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ARCHIVES OF OPHTHALMOLOGY.

STUDIES IN THE VIRUS OF HERPES SIMPLEX.[1]

BY DR. JONAS S. FRIEDENWALD.

(FROM THE LABORATORY OF PATHOLOGY OF THE MASSACHUSETTS CHARITABLE EYE AND EAR INFIRMARY, AND THE DEPARTMENT OF PATHOLOGY OF HARVARD MEDICAL SCHOOL.)

(With eight illustrations on Text-Plates III.–IV.)

INTRODUCTION.

THE subject of the ætiology of herpetic lesions is one that has, until recent years, been severely neglected by scientific investigators. As is usually the case when intensive study brings forth many new and important facts in a field that has long lain fallow, much of the recent discussion has been confused and encumbered by an inadequate and overlapping terminology. We shall, therefore, segregate from out of the mass of conditions clinically described as herpetic, two distinct groups of lesions *herpes zoster* and *herpes simplex*, and confine our discussion to them.

Of these two the former has long been recognized as a clinical entity. Epidemiological and clinical evidence recently gathered would tend to show that many, or perhaps all cases

[1] Read before the Harvard Medical Society, Boston, Mass., December 19, 1922. This work was undertaken at the suggestion, and conducted under the guidance of Dr. F. H. Verhoeff to whom the author is gratefully indebted.

of herpes zoster were due to an infection with a specific organism, and that this organism is closely allied to the causative agent of chicken-pox. In ever increasing numbers epidemics of chicken-pox are being reported in which the spread of the epidemic seems, with reasonable certainty, to have been traced to a case of herpes zoster as source. Cases of herpes zoster apparently contracted by contact with cases of chicken-pox have also, though less frequently, been reported. On the other hand, certain observers have noted as the result of careful general examination of patients suffering with herpes zoster, the frequent presence of isolated vesicular and pustular lesions scattered over the patient's body outside of the region involved in the zoster, and they describe these lesions as being in every way similar to those of chicken-pox. (Bibl. 1–9.) Experimental evidence is as yet lacking for the proof of this theory that herpes zoster and chicken-pox are both manifestations of infection with one and the same organism, but the infectiousness of herpes zoster has been demonstrated by Lipschuetz (39), who has produced herpes-like lesions in rabbits by inoculation with serum obtained from the vesicles of herpes zoster. This observation is, as yet, unconfirmed.

Herpes zoster is, then, a well defined clinical entity, but whether it is an infectious disease due to a single specific organism, while strongly suggested, has as yet not been proven conclusively. In the case of herpes simplex the opposite is true. Under this term we wish to embrace a considerable variety of clinical forms which we hope to show are produced by a single specific infectious organism. We propose to include under this head those cases of herpes occurring in the course of various febrile diseases and also labial or facial, genital, or corneal herpes, in general, excluding only herpes zoster. From the experimental side there seems to be no good reason for distinctions within this group.[1] Whether, as would seem likely, herpetic stomatitis also belongs to this group, has not as yet been proven, nor is it known whether or not herpetic lesions of this kind occur on the various internal mucous membranes. It is to the consideration of the ætiology of herpes simplex and not of herpes zoster that the rest of this paper will be confined.

[1] Exception should perhaps be made for genital herpes, see below.

Simple herpes and the corresponding forms of herpetic keratitis have generally been regarded as symptoms rather than as a specific disease entity, symptoms that might be produced by any one of a number of different ætiological agents. The frequent occurrence of herpes in various infectious diseases such as pneumonia, epidemic meningitis, malaria, multiple sclerosis, and infectious jaundice, as well as in many mild grippe-like infections, is well known. So also is the occurrence of herpes after intravenous and arsenical therapy, during menstruation, after dietary indiscretions, and even, as sometimes alleged, after emotional stress. It would seem difficult to assign any specific ætiology to a condition which occurs under such a wide variety of circumstances, but it should be remembered that herpes occurs perhaps most frequently as an isolated phenomenon, or at best associated with mild grippe-like symptoms,—congestion of the upper respiratory tract, slight general malaise, moderate psychic depression, and perhaps even a low fever. This last condition has sometimes been called "herpetic fever."

Though the theory of the symptomatic nature of herpes has gained general acceptance, not a few articles can be found in the literature disputing this notion, most notably those articles reporting epidemics of herpes simplex or herpetic fever. To cite only the most recent of such reports,—K. Mayer (10) describes an epidemic which broke out in an isolated company of troops. The company consisted of about 70 men, 6 officers. All men slept in one large room, the officers in one small room. The first case of herpes appeared among the officers. In the course of two weeks, 5 out of the 6 officers and about 30 of the men became affected. The appearance of the lesions was quite typical of ordinary herpes. Most of those affected complained of mild malaise but none was so ill as to be unable to perform his duties. The epidemic reached its height at the beginning of the second week and died out at the end of two weeks. No other disease was concurrently present in epidemic form. Zlocisti (11) has described a similar epidemic and reports in detail the clinical course of his cases, some of which were unusually severe. The existence of epidemics of this kind would naturally lead to the supposition that herpes is not merely a symptom but a specific infection. It is interesting, in this

connection, to note that there is a belief widely held among the laity that labial herpes is contagious. Popular beliefs of this kind are often based on sound though uncontrolled observation and deserve more respect than is generally accorded them by the profession.

HISTORICAL.

In the past few years a great wealth of experimental evidence has been brought forward tending to show that all the various forms of simple herpes are manifestations of infection with one single specific organism. In 1912–13, Grüter (35) found it possible to produce in rabbits a violent keratitis by inoculating their corneæ with scrapings from the lesions in a case of dendritic keratitis. It was possible, furthermore, to transmit this condition from one rabbit to another by successive inoculations. These observations were confirmed by Kraupa (37)

Loewenstein (40), and later Luger and Lauda (41) repeated Grüter's experiment and demonstrated further that an identical form of keratitis could be produced in rabbits by inoculation with material derived from any form of herpes simplex or herpes febrilis, either corneal, facial, or genital; *not*, however, from any form of herpes zoster. The technique of these inoculations was very simple. The herpetic bleb was cleaned off with alcohol and then incised with a sharp knife. This knife with the drop of serum clinging to it was immediately used to scarify in linear streaks, the cornea of a rabbit previously anæsthetized with cocaine. Later it was found that inoculation could also be successfully made if the contents of the herpetic bleb were suspended in salt solution and a knife dipped in this suspension was used to scarify the rabbit's cornea,—indeed the virus was found to be potent in amazingly high dilutions. The clinical course of the disease so produced in rabbits will be discussed below. These writers have noted that it bears many points of resemblance to dendritic and superficial punctate keratitis. By the aid of the immunity which is established in animals that have recovered from the disease they demonstrated the identity of the noxious agents which they had obtained from a great variety of herpetic

lesions.[1] Control experiments of simple scarification of the rabbit's cornea, and also inoculations from normal labial epithelium, from burn blisters, eczema pustules, etc., failed to produce the disease.

Loewenstein, and Luger and Lauda were able to transmit this disease from one rabbit to another with undiminished virulence. Guinea pigs were slightly susceptible, cats and dogs could not be infected. They found that the noxious agent obtained from the herpetic bleb or the infected animals' cornea could be rapidly destroyed by heat, less rapidly by cold, that it could not be preserved for 24 hours in salt solution nor in serum at incubator temperature. They were unable to demonstrate conclusively the presence of any visible micro-organisms, though Loewenstein described certain minute dots in stained smears from herpetic vesicles. He concluded that the organism belongs to the group of ultramicroscopic or filtrable viruses, and Luger and Lauda later succeeded in passing the virus through a Berkefeld filter. From their experiments these writers were convinced that they were dealing with a specific virus found only and always in herpetic lesions and causing herpes-like manifestations in experimental animals.

These authors reported, also, that certain of the infected animals developed symptoms of a severe general disease with paralyses and convulsions, often terminating in death. One cannot fail to note a strong analogy between this last observation and the findings of Levaditi and Harvier (18) who, working with a virus obtained from a case of epidemic encephalitis (lethargica) were able to produce in rabbits by corneal inoculation a keratitis followed by convulsions, paralyses, and death. Two questions now arose. *First*—is the fatal disease which

[1] Loewenstein failed to demonstrate the identity of facial and genital herpes in his immune experiments, and Lipschuetz was unable to infect guinea pigs with his strains of the virus obtained from genital herpes though these animals are at times susceptible to infection with the virus of facial herpes. The force of this argument is somewhat weakened by the fact that different strains of herpes virus vary greatly in their virulence for both rabbits and guinea pigs. Cushing (29) has reported a case in which facial and genital herpes developed simultaneously after operation on the gasserian ganglion.

occurs, at times, in rabbits whose corneæ have been inoculated with the virus of herpes due to that same virus or is it due to a secondary infection? *Second*—does any relation exist between the virus of herpes and the virus of encephalitis described by Loewe and Strauss (19), Levaditi and Harvier (18), and others? Both these questions have been answered in the affirmative.

Doerr and Vochting (30), and Doerr and Schnabel (31), and later others found that rabbits inoculated intracranially with herpes material regularly developed paralyses, convulsions, and died, and that this disease could be propagated from one rabbit to another by inoculating the second intracranially with an emulsion of the brain of the first, and that, further, after the virus had undergone several passages from brain to brain, it could be transferred to the cornea of a healthy rabbit and produce there a typical herpetic keratitis. Furthermore, animals which had recovered from a keratitis were immune to such intracranial inoculations. The two diseases are, therefore, caused by the same virus. The virus could be recovered also from the brains of animals that developed "encephalitis" after corneal inoculation.

Doerr and his co-workers next recovered a virus, from a case of epidemic encephalitis, which they found to be in every way identical with their herpes virus even to the establishment of complete cross immunity between the two. Blanc and Canninopetros (27), and Levaditi, Harvier, and Nicolau (38) were unable to confirm this last observation. They found that the virus of encephalitis with which they were working had consistently a greater virulence than the herpes virus, and that while animals which had been rendered immune to the encephalitis virus were immune also to herpes the converse was not true.

Levaditi, Harvier, and Nicolau discovered also a third virus, present in the saliva of 80% of normal persons, which partook of the common characteristics of the virus of encephalitis and that of herpes, but which was less virulent than either of these. This virus they named "virus salivaire keratogéne." They were able also, with any of these three strains, to produce skin lesions in rabbits having all the characteristics of herpetic skin lesions in man. They group these three viruses together with

those of rabies, polyomyelitis, and certain of the exanthems under the heading "ectodermotropic" since they all exhibit a marked selective affinity for ectodermal tissues and have, furthermore, certain other characteristics in common,—minute size, virulence in high dilutions, survival in glycerine, etc.[1]

EXPERIMENTAL.

The author felt that the observations of various workers summarized above, so contrary to the generally accepted theory of the ætiology of herpes, required first of all a careful repetition.

TECHNIQUE.

Material was obtained from herpetic lesions by the method described by Loewenstein (40). One or more linear scratches were made with the infected knife in the cornea of the animal to be inoculated. The scratches were made fairly deep, certainly going through Bowman's membrane. When the material to be inoculated had previously been suspended in liquid (either sterile normal salt or 50% glycerine) in addition to the scarification with the infected knife, several drops of the suspension were instilled into the conjunctival sac. At first whenever one eye of an animal was inoculated the other eye was also scarified in an exactly similar manner with a sterile knife and so served as a control. These controls resulted uniformly negatively and were, therefore, later omitted.

[1] For further articles by these and other authors consult bibliography.

It is, however, important to note in this connection that the authenticity of the virus of encephalitis has not been established beyond all question. Most investigators have found great difficulty in infecting rabbits with encephalitis material and since Oliver (23) and Wright and Craighead (24) have shown the existence of enzootic encephalitis frequently present among rabbits, the question arises as to whether the so-called virus of encephalitis is not merely a rabbit virus picked up in the course of frequent rabbit inoculations. The writer does not feel qualified to enter into this polemic, but the question as to whether or not a similar objection can be raised in relation to the virus of herpes will be discussed below. Doerr makes the interesting suggestion that the supposed virus of encephalitis may be merely the virus of herpes which has, as a secondary invader, entered the brain or spinal fluid of patients suffering with epidemic encephalitis.

RESULTS OF INOCULATION

No. of Cases	Source of Material	Result
	A. *Herpes*	
2	Facial herpes uncomplicated	2 positive
4	Facial herpes with slight "cold"	4 positive
1	Facial herpes with severe "grippe"	1 positive
2	Facial herpes with pneumonia	2 positive
1	Facial herpes with asthmatic bronchitis (material kept in salt solution for two hours before inoculation)	1 negative
1	Facial herpes following trigeminal neurectomy	1 positive
2	Dendritic keratitis	2 positive
Total 13	Total positive	12
	B. *Non-herpetic Conditions*	
2	Keratitis profunda disciformis	negative
2	Corneal ulcers, not herpetic	negative
2	Corneal phylctenules	negative
1	Rosacea keratitis	negative
1	Normal labial epithelium	negative
1	Pustule at lip margin	negative
1	Blister from electric burn	negative
1	Nasal and buccal secretion from normal	negative
2	Nasal and buccal secretions from cases of common cold	negative
1	Nasal and buccal secretions from a case of infected antrum	negative
1	Nasal and buccal secretions from a case of acute pharyngitis	negative (a streptococcus ulcer developed in the inoculated rabbit's cornea)
Total 15	Total positive	0

CONTROL EXPERIMENTS.

Control experiments were performed in relation to four possible sources of error:

(1) Trauma.

The reaction we were observing might be due merely to the trauma of inoculation. This possibility was eliminated by

frequent control experiments in which a rabbit's cornea was scarified with a sterile knife. In every such case the wound was completely healed in 48 hours.

(2) Local anæsthesia.

Loewenstein (40), and Luger and Lauda (41) used cocaine to anæsthetize the eyes of the rabbits which they inoculated. We found that the substitution of novocaine, holocaine, or general ether anæsthesia in place of cocaine in no way altered the results.

(3) The virus might be an invader of herpetic lesions, not their cause.

Loewenstein (40) and Luger and Lauda (41) conducted extensive experiments aimed to disclose this possibility. They inoculated rabbits with material obtained from a wide variety of non-herpetic lesions. All these inoculations failed to produce the typical reaction. They concluded that the virus was not present as a secondary invader in non-herpetic lesions.

The table given above confirms their results. See also Experiment II below.

(4) The virus might be a rabbit virus picked up in the course of the inoculations.

This possibility seemed to us particularly important because enzootic encephalitis is so very common among rabbits. Many of the pathological lesions found in the brains of rabbits inoculated with encephalitis material as described by Loewe and Strauss (19), and by Levaditi and Harvier (18) are not infrequently seen in supposedly healthy rabbits. This fact, as noted above, has been used with considerable force in the polemic over the supposed virus of encephalitis, and since that virus so closely resembles the one with which we are dealing the argument might be applied with equal force in our case. The following experiments were undertaken to discover whether by injuries of various sorts it was possible to induce a spontaneous infection of the herpetic type in a rabbit's cornea.

Experiment I.

Under cocaine anæsthesia the cornea of rabbit # 53 was exposed for ½ hour to the negative electrode of a storage battery (4 volts, 2–3 amperes). The current reached the cornea through a thread soaked in salt solution. At the end

of ½ hour a large area of the cornea was opaque, swollen, and denuded of epithelium. Immediately and again after 24 hours this injured cornea was inoculated with a mixture of the nasal and buccal secretions of two other healthy rabbits (# 40 and 45). During the next two days the eye became moderately congested but did not then nor later show the typical lesions. However an inoculation was made from this eye to rabbit # 41. Rabbit # 41 remained completely negative. Rabbits # 53 and 40 were subsequently shown to be susceptible to herpetic infection.

Similar experiments to this one were performed using bile, diphtheria toxin, and a protein to which the animal had been sensitized to produce the initial injury. In each experiment nasal and buccal secretions were obtained from different healthy rabbits. In no case was the resulting reaction at all similar to the typical herpetic infection and in no case was it transmissible to another rabbit. We were unable, then, to find, among healthy rabbits, carriers of the virus, though many of those we had used in these experiments were subsequently found to be susceptible to infection when inoculated either from human herpes or from infected rabbits.

Further evidence against the theory that the herpes virus is merely an enzoötic virus is to be found in the successful inoculation of man (see bibliography references 33, 34, 39); white rat (48) and guinea pig (41) reported by various writers.

TIME OF APPEARANCE OF VIRUS IN FACIAL HERPES.

In view of the suggestion that the virus with which we were dealing might be merely a secondary invader of the herpetic vesicle, it seemed important to discover how soon and how ong after the appearance of the herpetic lesion the virus could be detected.

Experiment II.

Case #10.—MacD. physician and co-worker with us in the laboratory who is subject to frequent attacks of labial herpes was requested to notify us at the very earliest appearance of an herpetic lesion. He presented himself one day stating that he had for the past two days felt a little poorly, he had been constipated and his head had felt "stuffy." He had had no nasal discharge, sneezing, nor fever. Two hours before he came to us he first noted a slight tingling and itching at a certain point on his lower lip. On examination a very slight hyperæmia and swelling was discovered in this region. Over its surface were scattered 3–4 minute

dew-drop like vesicles ¼*mm* in diameter. After cleansing with alcohol one of these vesicles was incised with a knife which was then used to inoculate the left cornea of rabbit #44. A typical keratitis developed. The lesion on the patient's lip proved also to be a typical herpes.

Experiment III.

Case #12.—A patient suffering with pneumonia at the Massachusetts General Hospital. Two weeks ago he had a cold in the head. Five days ago he developed a pain in the chest, cough, chills and fever, together with a severe pain on the left side of his face and the outbreak of a profuse crop of herpes. Examination revealed a large number of crusted lesions about his lips and on his left cheek. These bled easily when the crusts were lifted. Several of the crusts were removed and suspended in salt solution which was used ½ hour later to inoculate rabbit #43. A typical keratitis developed.

Clinical Course in Rabbits.

The clinical course of the disease in rabbits has been well described by Loewenstein (40), Luger and Lauda (41), and Doerr (30), (31), and his co-workers. We wish merely to record our confirmation of their findings.

The first signs of infection usually develop within 18–36 hours after inoculation. The incubation period may, however, be prolonged as much as 4 or 5 days. Such long incubation periods are usually associated with relatively mild infections, and can often be correlated either with an increased resistance of the host, as, for instance, when one eye of a rabbit is inoculated at a time when the other is already beginning to recover, or with a diminution in virulence of the virus, as, for instance, when the virus has been kept in normal salt solution on ice for an hour or more before inoculation. Examples of both these causes of prolonged incubation occurred several times in our series; however, several other cases of delayed reaction also occurred, in which no such explanation could be found, and in which the subsequent infection was by no means mild, indeed, in one case, unusually severe. Neglecting the occasional prolonged incubation the usual course of the infection is as follows:

Within 18–36 hours after inoculation the streak made in the cornea by the inoculating knife shows a number of minute irregularities along its margin as if it had been etched, and these irregularities on close examination are found to be due to minute superficial vesicles. After 48 hours a slight pericorneal congestion develops and the streak of inoculation becomes faintly opaque and stains readily with fluorescin, the line of stain having a number of circular excrescences at the sites of the vesicles which are now ¼–½*mm* in diameter, and have frequently shed their epithelium. On the third and fourth day the conjunctiva becomes markedly congested and swollen, a profuse purulent discharge develops, composed almost entirely of polymorphonuclear pseudo-eosinophilic leucocytes and fibrin. Smears from this pus stained by the gram or methylene blue stain do not show, up to the fourth or fifth day, any organisms. Later, various organisms, usually large gram positive cocci and bacilli, obviously secondary invaders, make their appearance. The opacity at the site of inoculation has in the mean time become more dense and wider, and a faint haze is often visible throughout the whole cornea. Fluorescin stain now reveals in addition to the original scratch numerous small circular spots scattered over the cornea ¼–1*mm* in diameter, strikingly similar to those seen in superficial punctate keratitis and also in dendritic keratitis in man. Some of these spots may coalesce to form larger areas. In addition to these there are almost always branching trunks extending out over the cornea from the original scratch. These dendritic and punctate lesions can, of course, be faintly seen without the aid of fluorescin but the stain brings them out with great vividness. A moderate iritis is often present. At this time and later the cornea often, though not invariably, exhibits a marked diminution in sensitivity.

After the fourth to seventh day the process begins to subside, the secretions become less profuse, the lids are covered with dry crusts, but in general the opacity and denudation of the cornea proceed for several days. The ultimate result for the cornea after a period of months may lie anywhere from the faintest opacity involving only the line of inoculation, to a dense leucoma involving the whole cornea. The latter may be due to a secondary infection.

Out of 58 rabbits successfully inoculated corneally, 12 developed encephalitic symptoms. Of these 6 died. The clinical course of these cases is as follows: From 7–14 days after inoculation the animal became irritable, starting at the slightest noise or touch, and at times rushed furiously and blindly about the cage. Some previously tame animals became quite ferocious at this period. All of them showed a very marked tendency to turn their heads toward the side of the affected eye. In the milder cases these symptoms passed off in 2–5 days. In others the animal developed paralyses of one or several limbs and severe opisthotonic convulsions. All those that manifested these grave symptoms died. Doerr and Schnabel (31) call attention to paralyses of eye muscles causing strabismus. We are, however, at a loss to know how strabismus can be detected in an animal which has no binocular vision. Profuse salivation as described by these authors occurred frequently, but not invariably, in our experiments. The virus can be found in the saliva of these animals.

Experiment IV.

Rabbit #65 was inoculated in both corneæ on March 17th with herpes virus (strain #10, which had already undergone 2 animal passages.)

March 20th. Violently inflamed eyes with profuse purulent discharge.

March 26th. Inflammation subsiding leaving a large opacity in each cornea.

March 27th. Same. Does not seem ill.

March 28th. Very ill, paralysis of right fore and hind legs, profuse salivation, frequent opisthotonic convulsions. Turns head to left, slow horizontal nystagmus of left, none of right eye, trismus, twitching of various muscles.

At this point an inoculation was made from the saliva of this rabbit to the cornea of a fresh rabbit, #70. The cornea of rabbit #70 was scratched with a sterile knife, and a cotton swab that had been dipped in the saliva of rabbit #65 was gently stroked over the scratches and some shreds of saliva were deposited in the conjunctival sac. An unusually severe but perfectly typical infection developed from which the virus was subsequently transmitted to other rabbits. Experiment I showing the absence of the virus in the saliva of normal rabbits serves as a control for this experiment.

It is interesting to note that the strain of herpes virus used in this experiment was by far the most virulent of those we encountered. It was obtained from a very severe case of dendritic keratitis.

According to Netter the virus of encephalitis can be found in the salivary glands of infected rabbits. Levaditi has been unable to confirm this view.

PATHOLOGY.

The tissues examined were fixed in Zenker's fluid, embedded in paraffin and stained with Wolbach's modified Giemsa stain.

EYE.

The pathological picture of the cornea varies greatly according to the stage of the infection. Eyes examined 24 hours after inoculation show along the line of inoculation, and in small foci close by, a disorganization of the normal relations of the epithelial cells with a disappearance of the columnar arrangement of the basal cells. Many of the cells are swollen and vacuolated. Some have fused together forming multinucleated giant cells.[1] In the nuclei of many cells the so-called "herpes-bodies" of Lipschuetz (39) are readily seen,—irregular masses of eosinophilic material gathered at the center of the nucleus and surrounded by a clear unstained zone. Chromatin network and nucleolus are completely lost from these nuclei. Whether or not these bodies are specific to herpetic infections as Lipschuetz claims, only future investigation can decide. The epithelium is in places raised by minute collections of fluid and, even in the early stages, has been shed over small areas.

Beneath Bowman's membrane there is an accumulation of polymorphoneuclear leucocytes which occasionally are seen to be eroding the membrane and migrating into the epithelium. They are arranged at times in densely packed groups, forming a small disk of infiltrate just beneath Bowman's membrane and producing a picture strikingly similar to that seen in superficial punctate keratitis as described by Verhoeff (14). At the limbus there is the usual inflammatory reaction consisting in

[1] First noted by Loewenstein (40).

marked congestion and an infiltration of polymorphonuclear leucocytes and small lymphocytes, the latter predominating.

In later stages (4th to 7th day) the cornea is widely but not deeply ulcerated. The polymorphonuclear infiltrate has increased in density about the margins of the ulcer. The pericorneal reaction is more marked. In extremely severe infections the whole thickness of the cornea may become necrotic as evidenced by the absence of corneal corpuscles. Only a few leucocytes are then found in the most severely affected regions but on the posterior surface of Descemet's membrane and raising up the endothelium they are then present in a dense layer. In such unusually severe infections the iris is found to be moderately infiltrated with lymphocytes and polymorphonuclear leucocytes and its capillaries are widely dilated. No lesions were found in the lens, vitreous, retina, choroid, or optic nerve.

BRAIN.

The pathology of the brain in this condition has been described in detail by Doerr and Schnabel (31) and by Levaditi, Harvier, and Nicolau (39). The lesions found resemble those seen in human epidemic encephalitis, but it should be remembered that identical lesions are found occasionally in supposedly healthy stock rabbits. We have seen these lesions in both infected and control rabbits. They consist in perivascular round cell infiltrations, slight chronic meningitis, small foci of round-cell infiltration in the gray matter usually surrounding degenerated ganglion cells. We did not find the organisms observed by Wright and Craighead (24) in the enzootic encephalitis that they have described. In our short series of observations we found these lesions much more common in infected than in control animals but we would be far from suggesting that they represent the specific pathology of this disease.

The pathology of the gasserian ganglion and trigeminal nerve will be described below.

PATH OF VIRUS FROM CORNEA TO BRAIN.

Doerr and Schnabel (31) believed that the virus reaches the brain from the cornea by means of the blood stream and they

were able to isolate the virus from the heart's blood of a severely infected animal. Levaditi, Harvier, and Nicolau (38) have thrown some doubt on this conclusion by showing that the resistance of the mesodermal tissues of the animal's body is very high for this virus, and that infection is as a rule possible only if the virus is introduced into ectodermal tissue—skin, cornea, brain, or peripheral nerves. Indeed, animals readily withstand huge doses of the virus given intravenously. These authors believed that the virus entered into the interior of the eye and reached the brain by way of the optic nerve, and they were able to demonstrate the presence of the virus in the aqueous fluid and optic nerve a certain number of days after infection of the cornea. These experiments were done with the virus of encephalitis, not that of herpes.

While not being in a position to refute this theory we must nevertheless state that it seems to us highly improbable that any large number of organisms should pass through an intact membrane of Descemet or that they should multiply in the interior of the eye and along the course of the optic nerve without attracting leucocytes and producing pathological evidence of their presence. No such evidence has been adduced by these authors, and repeated examinations by us of the interior of the eye and of the optic nerve failed to reveal anything except a deposit of leucocytes on the posterior surface of the cornea and a mild iritis such as one would naturally expect as the result of a severe corneal infection.

From the human side there is much evidence pointing to an intimate relation between herpetic infections and the sensory nerves, in particular the trigeminal nerve. In fact febrile herpes occurs but rarely outside of the genital regions and the domain of the trigeminal nerve. Hypæsthesia of the cornea in cases of herpetic keratitis in areas not visibly affected, and hypæsthesia and hyperæsthesia of the areas involved in facial herpes after the subsidence of the infection are well known and point strongly to an involvement of the sensory nerves.

Cushing (29) has pointed out that herpes very commonly follows operations on the gasserian ganglion in cases of trigeminal neuralgia and he states that when the ganglion is removed herpes are rare, but when a peripheral branch is cut, herpes frequently appear on the opposite side or in the domain

ILLUSTRATIONS

ILLUSTRATIONS.

Figure 1. Furrow of inoculation in rabbit's cornea after 24 hrs. Section cut slightly on the bias. High dry magnification. *F.* furrow of inoculation. *H.* herpes bodies. *G.* giant cell. *S.* corneal stroma.

Figure 2. Very early lesion showing polymorphonuclear accumulation beneath Bowman's membrane and changes in the epithelium. *E.* epithelium. *S.* stroma. *G.* giant cell. *P.* polymorphonuclear leucocytes. High dry magnification.

Figure 3. Advanced lesion (8 days) with ulceration and necrosis of cornea and marked Descemetitis. *D.* Descemet's membrane. Note the practical absence of corneal corpuscles in the lower layers of the cornea. Most of the nuclei in the upper layers are those of polymorphonuclear leucocytes. Low power.

Figure 4. Perivascular infiltrate in brain. Low power.

Figure 5. Focus of small round cells in a ciliary nerve. High dry power.

Figure 6. Gasserian ganglion showing first type of lesion. *N.* normal ganglion cell. *A.* abnormal cell. High dry power.

Figure 7. Higher magnification of same specimen as figure 6.

Figure 8. Gasserian ganglion showing second type of lesion. *G.* degenerated ganglion cells. High dry power.

ILLUSTRATING DR. JONAS S. FRIEDENWALD'S ARTICLE ON "STUDIES IN THE VIRUS OF HERPES SIMPLEX."

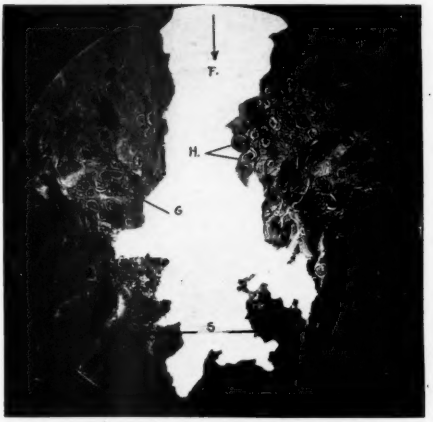

FIG. 1

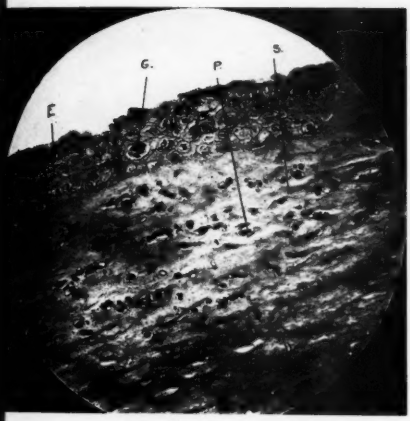

FIG. 2

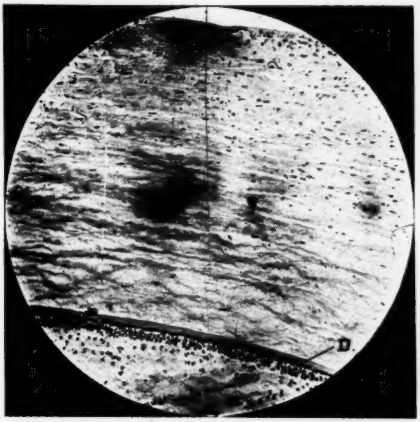

FIG. 3

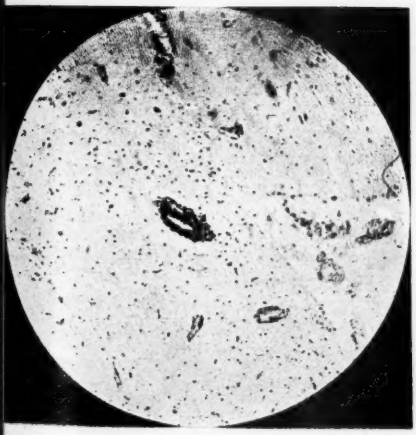

FIG. 4

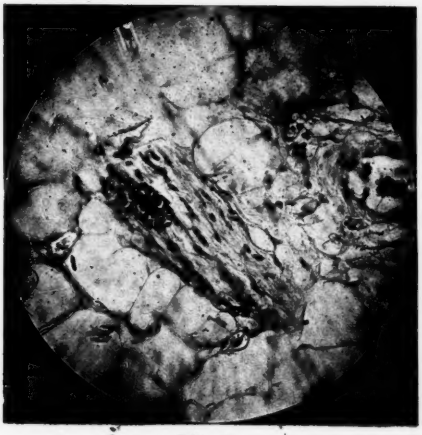

FIG. 5

ILLUSTRATING DR. JONAS S. FRIEDENWALD'S ARTICLE ON "STUDIES IN THE VIRUS OF HERPES SIMPLEX."

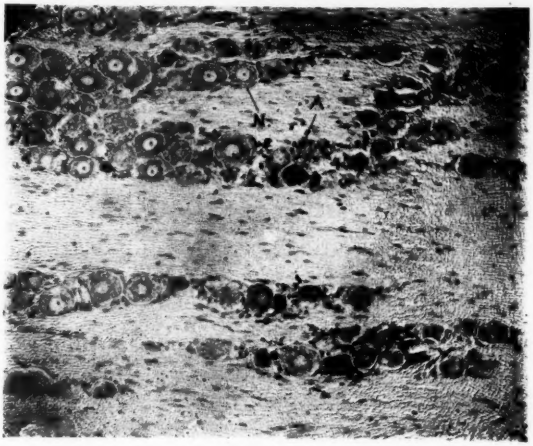

FIG. 6

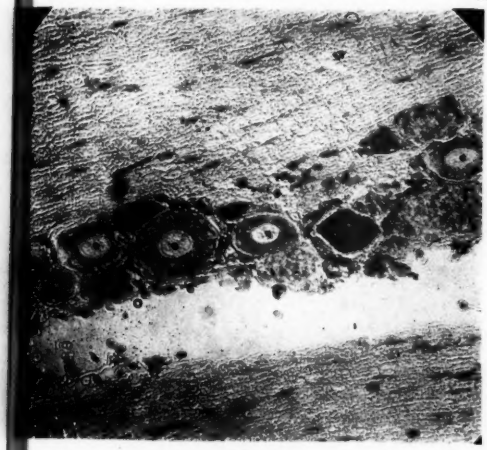

FIG. 7

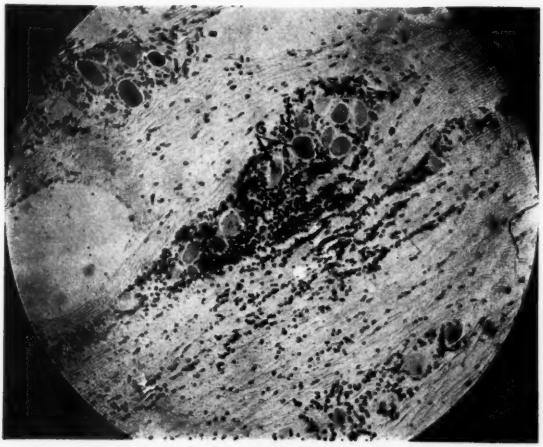

FIG. 8

of one of the uninjured branches. This would point strongly to the ganglion as the focus of the infection whence the virus travels peripherally or centrally.[1] Furthermore Howard (13) has observed lesions in the gasserian ganglia of patients with herpes complicating pneumonia and epidemic meningitis and Gilbert (12) has seen lesions in the ciliary nerves of a case of herpetic keratitis. A final and important bit of evidence from the human side is the close similarity between the lesions in febrile herpes and herpes zoster; the latter is known to be an affection of the sensory ganglia and their peripheral nerve fibers.

These considerations led us to investigate what part, if any, the gasserian ganglion and trigeminal nerve played in the disease in rabbits.

1. The presence of the virus of herpes in the gasserian ganglia of rabbits whose cornea have been infected.

Experiment V.

Rabbit #73 was inoculated in both eyes with a virus (S 10) which had already undergone 5 successful animal passages. The typical corneal lesions developed from which, on the fourth day, the virus was recovered and successfully inoculated into rabbit #71.

Three days later, namely on the seventh day after inoculation, the corneal lesions were subsiding, leaving large opacities. The rabbit seemed in no way ill, he was eating well, and showed no evidences of paralyses. He was killed and the right gasserian ganglion was removed, emulsified in salt solution, and inoculated into the cornea of rabbit #74. This rabbit developed a perfectly typical and severe keratitis

[1] The reader may have some difficulty in accepting the notion that herpes following operation on the trigeminal nerve is due to a virus. It cannot however, be due merely to trauma since, as stated, the herpes commonly appears in the domain of the uninjured nerve. The outcropping of herpes in these cases is commonly associated with slight fever, sometimes with signs of mild meningeal irritation and increased cell count in the spinal fluid,—all factors pointing to an infection. We have, moreover, recovered the virus from the facial herpes of such a case. If, as seems indicated, the herpes virus is frequently present in the gasserian ganglia of persons suffering with trigeminal neuralgia one may well ask is it present also in the ganglia of normal persons, and what is its possible relationship to the tic douloureux.

and from his cornea the virus was successfully inoculated into other rabbits.

2. Pathology of the gasserian ganglion and ciliary nerves. At various intervals after corneal inoculation, both before and after the development of symptoms of cerebral infection, rabbits were killed and their gasserian ganglia were subjected to microscopic examination. Every ganglion so examined showed lesions not found in normal controls. The lesions were of two types.

The first type of lesion was confined to the ganglion cells. Scattered among perfectly normal looking cells one found here and there a ganglion cell whose cytoplasm was considerably shrunken and packed with very dense masses of deeply staining basophilic material. Various degrees of this condition are seen in one and the same section, from cells which seem to have merely an unusually large amount of the normally present Nissl bodies to cells which appear as solid almost structureless deeply staining masses, their nuclei being wholly obscured. These basophilic masses are irregular in shape, hazy in outline, and without internal structure, and could not be confused with the intracellular masses of organisms in the enzootic disease described by Wright and Craighead.[1]

The second type of lesion presents a more familiar picture. Here we see the ganglion infiltrated with small round cells which are found forming a mantle about the venules and capillaries and surrounding, and at times invading, degenerated ganglion cells,—namely ganglion cells which have almost completely lost their staining properties and from which the nuclear outline has completely or almost completely disappeared. The picture is identical with that seen among the anterior horn cells in poliomyelitis.[2]

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[1] Since the completion of this work my attention has been called to the fact that there exist in normal sensory ganglia two types of ganglion cells which can be differentiated by various special stains as chromophile and chromophobe. I am not now in a position to repeat the experiments which I am reporting and therefore feel a certain hesitancy in maintaining that the deep staining cells are a pathological finding. However, the fact remains that they were not to be found in the controls which I instituted at the time.

[2] This type of lesion has been described by Stocker (47).

Not infrequently the two types of lesions are simultaneously present. Their interpretation is a matter of much difficulty, but it would seem probable that the shrunken dark staining cells are in the process of reacting to the growth of the virus along their peripheral axones, while the inflammatory lesions are produced by the actual presence of the virus in the ganglion itself. That pathological influences are acting along the course of the sensory nerves can be seen in the sections of the orbital tissue which not infrequently reveal foci of small round cells imbedded in some of the ciliary nerves.

In view of this demonstration of the intimate relation of herpetic infection to the sensory nerves it becomes important to consider the mode of entry of the virus in human cases. Levaditi (38) and Doerr (31) have shown that the virus of herpes is sometimes present in the buccal secretions of persons suffering with herpes and also of some normal individuals who may reasonably be supposed to be carriers of the disease. This, together with the clinical fact that the onset of herpes is so commonly associated with a mild or severe upper respiratory infection, would lead one to conclude that the portal of entry lies somewhere in the upper respiratory passages. No evidence is on hand to indicate whether the virus in human infections reaches the nerve from the mucous membrane directly or via the blood stream. It should be remembered in this connection that in many individuals the maxillary branch of the trigeminal nerve lies in the roof of the maxillary sinus covered only by mucosa. It is in the domain of this branch that febrile herpes most commonly occur.

Dr. F. H. Verhoeff has suggested that the virus of herpes may be a cause of optic neuritis, especially of those cases of retrobulbar optic neuritis in which the ophthalmologist is led to suspect the nasal sinuses but the rhinologist unable to demonstrate any lesion.

HERPES IN MAN AND RABBITS.

A short comparison of the course of herpetic infection in man and rabbits may perhaps be of interest. Herpetic (herpes simplex) skin lesions in man are acute and of short duration as in rabbits. Corneal herpes, however, is in man a subacute

affection often of extremely long duration, while in rabbits it is acute and always begins to subside within a week. Neglecting this difference which can readily be accounted for by the difference in resistances of the hosts the corneal lesions in man and rabbit are strikingly similar. Lipschuetz (39) has found "herpes bodies" in the epithelial cells in human herpes of the skin, and Fuchs and Lauda (34) have found them in corneal herpes in man artificially produced in an eye about to be enucleated for some other cause. The similarity of the distribution of the corneal infiltrate in rabbit infection to that seen by Verhoeff (14) in superficial punctate keratitis in man has been noted above. Gilbert (12) found a neuritis and perineuritis of the ciliary nerves in a human case and Howard (13) has described inflammatory lesions in the sensory ganglia corresponding to areas involved in herpes. In spite of careful search we were unable to find budding capillaries in the irides of infected rabbits similar to those noted by Verhoeff (14) in his case of superficial punctate keratitis.

Whether or not herpetic encephalitis occurs in man as in rabbits it is at present impossible to say. Symptoms of meningitis have been frequently noted in cases of herpes, supposedly herpes zoster but possibly merely unusually severe cases of herpes simplex.

Levaditi and others believe that all cases of epidemic encephalitis are what we have called "herpetic encephalitis," namely that the virus of encephalitis is merely a herpes virus of unusual virulence. Notwithstanding his desire to support this hypothesis Netter was unable to find herpes in more than 2% of a large number of cases of encephalitis. Experience with the disease in rabbits would lead one to expect just such a condition as Netter found. If herpes and encephalitis are manifestations of infection with the same organism one would not expect them to be simultaneously present but one would look for the herpes during the second week or perhaps even the third week *before* the onset of the encephalitis.

THERAPY.

We had found that the corneal infection of rabbits ran its course with great regularity, and little variation was seen in

the severity of the disease when rabbits of equal size and age were inoculated at the same time from the same source. In particular if a rabbit was inoculated in both eyes the reaction of the two eyes was found to be practically identical. Here then was an obvious and easily controlled method for determining the value of various therapeutic agents. The study was limited to local applications of various medicaments.

SUBSTANCES TESTED.

Argyrol	25%	instilled every 2 hours.
Mercurochrome	1%	" " " "
Holocaine	1%	" " " "
Zinc Sulphate	0.25%	" " " "
Cocaine	4%	" " " "

Tincture of Iodine full strength applied daily for 2 or 3 days after anæsthetizing cornea with cocaine.

Ox bile (Fel bovis U. S. P.) approx. 10% applied daily for 2 or 3 days after anæsthetizing cornea with cocaine.

METHOD.

Both eyes of a young rabbit were inoculated simultaneously from the same source. Twenty-four to 48 hours after inoculation treatment was begun with the drug to be tested, one eye being treated, the other being kept as a control. Treatment was continued until the height of the disease had been passed and the condition was subsiding. Records were kept of the severity of each symptom,—blepharospasm, congestion, secretion, corneal anæsthesia, opacity, area stainable with fluorescine, etc., together with the duration of the illness until disappearance of all congestion, and the amount of opacity at that time.[1]

RESULTS.

We regret to report that the results of these experiments were wholly negative. None of the substances used were seen to have the slightest beneficial effect on the course of the disease

[1] In later experiments for the sake of economy, 3 or 4 rabbits were inoculated at one time and all but one or two of the infected eyes were treated, the remainder constituted the control.

in rabbits. Cocaine in the strength used and ox bile were both definitely harmful. The demonstration of the deleterious effect of cocaine is in accord with clinical experience and is analogous to the findings of Levaditi, Harvier, and Nicolau who showed that general anæsthetics, chloral, ether, and chloroform, greatly increased the severity and shortened the incubation period of the disease produced in rabbits by the virus of encephalitis.

It is not easy to translate these findings into terms relating to the treatment of herpetic keratitis in man because the disease runs a much more acute and severe course in rabbits, giving less opportunity for successful treatment, however it seems beyond question that none of the remedies used are in any sense specific for the disease, that they can hardly be more than mild palliatives and that at the present stage of knowledge vigorous treatment would be contraindicated. The frequent use of cocaine should be avoided.

CONCLUSIONS.

1. Herpes simplex in both its corneal and facial manifestations is due to a specific virus.

2. This virus is found constantly in the lesions of herpes simplex but not in lesions of any other condition examined.[1] It can be found in the herpes at the time of their earliest appearance, during the vesicular stage, and, at times, in late crusted lesions.

3. The virus is highly infectious for rabbits, causing in them a disease which in many respects resembles herpetic keratitis in man.

4. A certain number of rabbits whose corneæ have been infected with this virus develop an acute and often fatal encephalitis.

5. The pathology of experimental herpetic keratitis in rabbits resembles that of herpetic keratitis in man.

6. The path of the virus from the cornea of a rabbit to its brain is probably along the sensory nerves of the cornea.

7. Treatment of experimental herpetic keratitis by the

[1] Other workers have found the virus to be occasionally present in the saliva of normal and infected persons.

methods usually used in the treatment of herpetic keratitis in man produced no favorable effect on the course of the disease. The use of strong solutions of cocaine produced a deleterious effect.

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A CASE OF MESOBLASTIC LEIOMYOMA OF THE IRIS.

By Dr. F. H. VERHOEFF.

(From the Massachusetts Charitable Eye and Ear Infirmary.)

(With three illustrations on Text-Plate V.)

IN the literature there have been described as myomata of the iris, three tumors, and as myomata of the ciliary body, six tumors. In addition to these, a tumor described by Dreschfeld as a sarcoma of the iris has been regarded by some observers as a myoma. In none of these cases was conclusive evidence brought forward that the tumor was really a myoma, so that considerable doubt exists as to whether or not a myoma of the uveal tract has ever actually occurred. In the following case of tumor of the iris, the general character of the cells as shown by ordinary stains together with the presence of myoglin fibrils as demonstrated by differential staining, leave no doubt that the tumor was a myoma. For the privilege of reporting the clinical features of this case I am indebted to Dr. Myles Standish.

Case:

Martin K. S., aged 33, admitted to the Massachusetts Charitable Eye and Ear Infirmary, May 21, 1904, service of Dr. Standish. The patient states that a growth has always been present on the iris of his left eye but that it has doubled in size within the past two years. Examination: Right eye normal, vision = $\frac{20}{15}$. The left eye is also normal, except for the presence of a tumor in the anterior chamber, and its vision is normal. The tumor is situated in the lower outer quadrant, extends from beneath the corneal limbus to the pupillary margin, measures about 5*mm* x 4*mm* in size, and is in contact with the cornea. No connection of the tumor

ILLUSTRATING DR. F. H. VERHOEFF'S ARTICLE ON "A CASE OF MESOBLASTIC LEIOMYOMA OF THE IRIS."

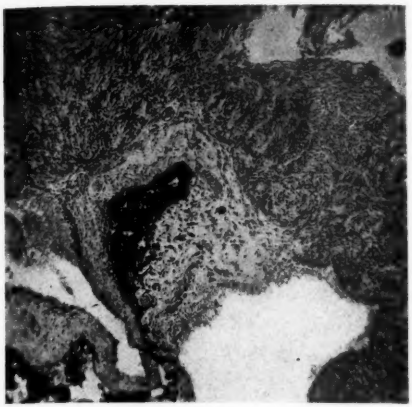

FIG. I

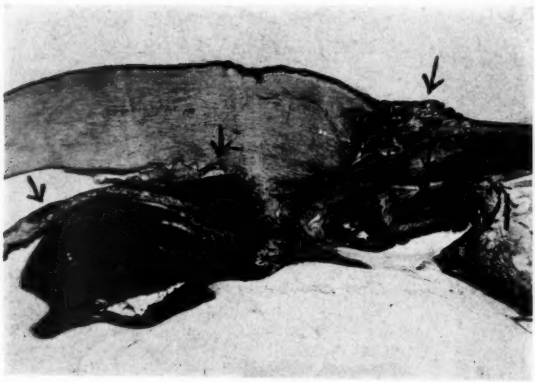

FIG. 2

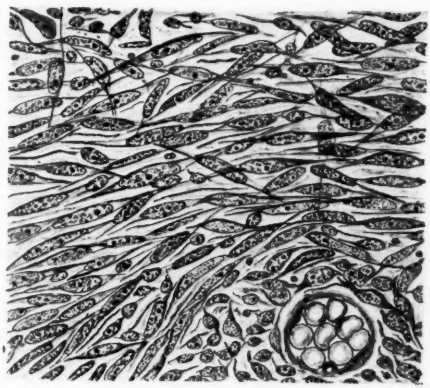

FIG. 3

with the iris can be definitely seen, but apparently it is connected with the latter near its root.

The tumor is pinkish in color, and, as seen with the corneal loup, has a papillary appearance, each process containing a loop of blood vessels. There is a small hemorrhage on the surface of the tumor and a small hyphemia at the bottom of the anterior chamber.

Operation.—Ether Narcosis.

Incision made through sclera 1½*mm* behind limbus below site of tumor. Root of iris grasped with forceps, pulled out and excised. Tumor, apparently completely removed with iris, preserved for microscopic examination.

May 22d. A large portion of the tumor still remains within the eye, so much, in fact, that the impression is given that none of the tumor has been removed.

Operation.—Wound reopened and another unsuccessful attempt made to remove the tumor with forceps. Suction instrument then used, also without success.

May 23d. Anterior chamber reformed.

May 24th. Within the coloboma the tumor appears as an irregular gray mass entirely unconnected with the iris or ciliary body. Eye considerably congested. Discharged.

The patient then consulted Dr. Standish privately, from whose records the following notes were obtained:

July 23, 1904. Eye quiet. The tumor looks solid and lobulated and measures 5*mm* x 2*mm* in size. It has become vascularized by vessels extending from beneath the corneal limbus.

Dec. 19, 1905. Tumor 3*mm* x 2*mm* in size. Patient states that there has been a hemorrhage into the anterior chamber since previous visit.

Oct., 1908. Unchanged.

March 12, 1920. Patient states that three years ago the growth began to increase in size. There have been several hemorrhages in the eye of late. The growth is pinkish in color and lies in the coloboma free from the iris, but at the periphery has a thin pedicle which extends beneath the limbus. V. O. S. $\frac{1}{15}$. V. O. D. $\frac{1}{15}$.

March 24, 1920. *Operation.*

Incision made with broad bent needle at site of former incision. Attempt to remove tumor with forceps failed, owing to softness of mass. Attempt with hook also failed. Tumor finally expressed with a spoon, leaving only the thin pedicle behind. A small amount of vitreous (lens matter?) lost.

April 8th. Lens cataractous and swollen. Marked congestion.

April 16th. Tension subnormal.

April 24th. Less congestion.
May 17th. Less congestion.
May 19, 1920. Tension very low. Enucleation.

PATHOLOGICAL EXAMINATION.

(857) First specimen: The specimen consists of a piece of iris with tumor attached, the latter measuring 4.25*mm* in diameter. Fixation in Zenker's fluid.

Microscopic Examination.—The tumor is attached to the iris, some distance from the iris root, by a greatly constricted base about 1*mm* in diameter (Fig. 1). It arises sharply from the anterior boundary layer and has not invaded the iris stroma. It is composed of long spindle-cells arranged in bundles running in various directions. The nuclei are long and rod-shaped and some of them are slightly curved. They measure 15 to 20 microns in length and 2.5 to 3.3 microns in thickness. When seen under high magnification, each cell is found to terminate in a long process. These processes give the tissue a highly fibrillated appearance. The nuclei show a marked tendency to arrange themselves in rows within the bundles, so that the appearance of alternate zones of nuclei and fibrils is often produced. Sections stained in phosphotungstic acid hematoxylin show definitely stained fine fibrils running along the borders of the cells and the processes (Fig. 3).

The tumor is only moderately vascularized. All of the vessels have definite connective tissue walls as shown by Mallory's connective tissue stain, no blood spaces being found which are bordered directly by tumor cells. The tumor cells have no constant arrangement with respect to the vessels, but occasionally they encircle the larger vessels. The connective tissue stain shows no collagen between the tumor cells except at the base of the tumor where a few collagen fibrils extend for a very short distance from the iris into the tumor.

None of the spindle-cells is pigmented, but a few (five in one section) typical branching chromatophores are found between the spindle-cells near some of the blood vessels. These no doubt originally belonged to the iris. The tumor shows no capsule in the sections, but its surface is ragged, indicating that a part of the tumor, including the original surface, has been torn off in the removal of the tumor. No mitotic figures are found.

The iris, in general, is normal. In places the anterior boundary layer is thickened as is often the case in a normal iris, and contains more pigment cells than elsewhere. At

the base of the tumor, the stroma contains numerous clump cells.

SECOND SPECIMEN REMOVED 16 YEARS LATER.

This consists of several fragments of tumor tissue. Fixation in 10% formalin. Microscopic examination shows the tumor to have the same structure as in the first specimen except that the cells are, in general, somewhat larger. No mitotic figures are found. None of the cells is pigmented.

THIRD SPECIMEN.

This consists of the entire eye. Fixation in 10% formalin.

At the limbus there is a healed operative wound. The cornea in the vicinity is vascularized and swollen to twice its normal thickness but is free from infiltration with inflammatory cells. Incorporated within the wound there are a number of small circumscribed nodules of tumor cells (Fig. 2). Some of these nodules are just beneath the surface epithelium. They consist entirely of unpigmented spindle-cells. The iris is absent in this situation and a mass of granulation tissue extends from the inner portion of the wound into the lens, the capsule of which has been ruptured. The lens is here considerably infiltrated with endothelial phagocytes, but no pus cells. At one side of the wound where the iris is present there is a flat sharply circumscribed nodule of tumor cells filling the filtration angle. This is composed of unpigmented spindle-cells and is $\frac{6}{10}mm$ in diameter. It has not invaded the ligamentum pectinatum. On this side several discrete tumor nodules of spindle-cells are found involving the surface of the iris. On the side opposite the wound there is one large nodule situated exactly at the pupillary margin and several minute nodules towards the periphery. All of the nodules have smooth surfaces. Some of them are sharply deliminated from the iris stroma, but others send short irregular projections into it. The cells of the larger nodules are as large as those of the original tumor, but the cells of the smaller nodules are correspondingly small in size. The tumor cells have nowhere become free and infiltrated the neighboring tissues. The iris stroma shows slight fibrosis and the surface of the iris has groups of endothelial phagocytes adherent to it. The pupil is closed by a vascularized membrane which extends from the pupillary margin over the lens. The lens, in addition to the infiltration already mentioned, shows the usual changes of a recent traumatic cataract and an anterior capsular cataract. Near the wound the swollen cortical matter protrudes through the gap in the capsule and presses against the cornea. Between the lens matter and the cornea are several nodules of tumor cells.

The tissues about the filtration angle have nowhere been

involved by the tumor and, except in the vicinity of the wound, the angle is freely open.

The ciliary body is congested and edematous but is free from cellular infiltration. Adjacent to the site of the iris coloboma as well as elsewhere the ciliary body shows no indication that the tumor has ever been attached to it. At the site of the wound the ciliary processes are adherent to the fibrous tissue extending from the latter, and the whole ciliary body has been folded and dragged forward by the resulting traction. On the opposite side the ciliary body has also been dragged forward by traction of the iris, but to a less extent.

On the side of the wound, and to a less extent on the opposite side, the choroid and posterior part of the ciliary body are separated from the sclera by a serous exudate. The choroid is congested throughout. The retina is *in situ* and normal except near the disk where it is edematous. The optic disk is greatly swollen but is free from cellular infiltration.

REMARKS.

The feature of chief interest in this case is that it is the first in which a tumor of the iris has been demonstrated by means of special staining to be a myoma. Even after ordinary staining, the long spindle-shaped appearance of the cells, their typical rod-shaped nuclei, and the tendency of the cells to occur in bundles with the nuclei arranged in rows, strongly suggested a myoma, but the presence of fibrils coursing along the cells and their terminal processes, as shown by Mallory's phosphotungstic hematoxylin stain, left no doubt as to the nature of the growth.

So far as I know, no attempt to ascertain whether or not fibrils occur in relation with the cells of spindle-cell sarcomata of the uvea, has hitherto been recorded. It may be well for me to state, therefore, that I have examined sections of a number of spindle-cell sarcomata of the choroid and ciliary body stained in Mallory's phosphotungstic and hematoxylin and have failed to find any fibrils in relation with the tumor cells proper. I have, however, found fibroglia fibrils in the connective tissue stroma.

In addition to the character and arrangement of the nuclei and to the presence of myoglia fibrils, I find another important

difference between myomata and uveal spindle-cell sarcomata. This consists in the fact that myoma cells are truly spindle-shaped whereas the cells of a uveal spindle-cell sarcoma are seldom if ever distinctly spindle-shaped but terminate in or send off laterally several ill-defined irregular processes which anastamose with neighboring cells and thus form a more definite syncytium. This syncytium is most easily recognizable where the cells are cut in cross section. In the case here reported this difference from a sarcoma is very apparent.

An especially noteworthy feature of this tumor is its slight malignancy as evidenced by the following facts:

1. That although a large portion of the growth was left in the anterior chamber at the first operation, it did not increase appreciably in size for a period of sixteen years. It is remarkable that the tumor remained alive in spite of the fact that its connection with the iris was completely severed. Its new blood vessels were evidently derived, not from the ciliary body, but from new tissue formed at the site of the operative wound. The dissemination of the tumor in the form of small nodules on the surface of the iris did not necessarily indicate malignancy, since this probably resulted from the operative traumatism.

2. That the original tumor arose from the surface of the iris by a small constricted base. This seems to be a point of difference from sarcomata that may prove of clinical value.

3. That the original tumor had not invaded the iris stroma.

4. That the tumor showed no mitosis.

6. That after sixteen years the tumor had not involved the structure at the filtration angle. This is in marked contrast to sarcomata of the iris which, under similar conditions, invade the ligamentum pectinatum and canal of Schlemm and extend along the emissary veins of the latter.

In a normal eye smooth muscle is derived from the pigment epithelium of the iris as in the case of the dilatator and sphincter pupillæ, or from the uveal stroma as in the case of the ciliary muscle. The question therefore arises as to whether the tumor in the present case was epiblastic or mesoblastic in origin. Since the tumor arose from the anterior surface of the iris near its root, was entirely unpigmented, and was nowhere connected with the iris muscles or pigment epithelium, it

seems likely that it originated from stroma cells of the embryonic uvea, possibly from misplaced cells which ordinarily would have taken part in the formation of the ciliary muscle.

In regard to the question as to whether any of the tumors previously described as myomata of the iris or ciliary body were really such, it is impossible, in the absence of differential staining, to arrive at a positive conclusion. It is reasonably certain, however, that the tumor described by Thompson and examined microscopically by Griffith was a true myoma. The spindle-cells were arranged in bundles and possessed rod-shaped nuclei. While many such nuclei may often be found in spindle-cell sarcomata, the nuclei are not predominatingly rod-shaped. In addition to this, the illustration of this tumor shows that there was a definite tendency for the nuclei to be arranged in rows leaving zones free from nuclei. There is some probability that the tumor described by Van Duyse was also a myoma of the iris, owing to its long duration, 20 years, and to its not having produced glaucoma or affected vision. From the meager histological description of this tumor, however, it cannot be differentiated from a spindle-cell sarcoma.

Owing to the fact that the ciliary body consists largely of smooth muscle, it would seem that a myoma, was more likely to occur here than in the iris. In none of the six cases of supposed myoma of the ciliary body reported, however, is it possible from the histological description given, to be reasonably sure that the tumor was not a spindle-cell sarcoma. In fact, I regard it as almost certain that the tumors were all spindle-cell sarcomata.

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REPORT OF A CASE OF AMAUROTIC FAMILY IDIOCY IN AN INFANT OF NON-JEWISH PARENTAGE.[1]

By Dr. MARTIN COHEN, New York City.

IN the year 1881, Warren Tay (1), an English oculist, presented to the Ophthalmological Society of the United Kingdom, a twelve-months old child who displayed "symmetrical changes in the region of the yellow spot in each eye." Tay stated that the child had been brought to his clinic because of a gradually increasing muscular weakness, first noticed when only two or three weeks old. Because he believed the cerebral development to be insufficient, Tay examined the eyes with the ophthalmoscope to ascertain if there was any affection of the optic nerve, which resulted in the findings which he called to the attention of the Society.

This is apparently the first case of amaurotic family idiocy to be placed on record. Three years later Tay reported two more cases occurring in the same family, and the next year a fourth case, in another family. The mother of this last infant stated that an older child had died at the age of fifteen months, after developing similar symptoms. All these infants were males, the offspring of Jewish parents.

In 1885 Goldzieher (2) of Buda-Pesth and Magnus of Breslau each reported a case, but the most important contribution to the history of this obscure disease concerned a case which occurred in this year, but was not fully reported until two years later. This patient was first seen by Herman Knapp of New York when four months old. She died at the

[1] Read before Section on Ophthalmology, New York Academy of Medicine, November 20, 1922.

age of two years, and an autopsy was performed by Bernard Sachs, who reported his findings in a comprehensive paper, entitled *Arrested Cerebral Development.* The chief pathological change consisted in an atrophy of the cerebral convolutions, with marked alterations in the shape and appearance of the large and small pyramidal cells of the cortex. The spinal cord and eyes were not examined. In 1898, Ward A. Holden (11) published a report on the microscopical eye-examination of Dr. Hirsch's case, which is an important contribution to this subject.

Sachs (3) at the time he published his account, was unaware of the earlier work done by Tay. He gave the designation *Amaurotic Family Idiocy* to the symptom-complex which he described, the eye-findings which had been Tay's chief interest being but one manifestation of the condition. Sachs was the first to recognize the familial element in the disease, and in his later publication (1910) made the statement that "the infantile form invariably occurs among Hebrews and among them only"; a peculiar circumstance apparently first noted by Carter (4) sixteen years before.

The priority of Tay's observation and the investigations of Sachs were recognized by Higier (5) who called the condition *Tay-Sachs'* disease, the name by which it is still frequently designated. The recognized symptom-complex at this time was the *familial* factor especially, associated with the eye-findings—"cherry-red" spot at the macula—the progressive mental impairment, the occurrence of the condition solely among children of Jewish parentage, and the period of life at which the disease began—from the third to the sixth month —making it peculiar to infants.

Up to 1917, about one hundred cases of *infantile* amaurotic family idiocy had been reported in the literature. In 1905, however, Vogt, Spielmeyer and others described a familial disease which clinically and in its histology and pathology closely resembled the condition described by Tay and Sachs, but differed from it, in that the symptom-complex was not manifested until the patient was past infancy, and that he often lived for a number of years, and also that the victims were not confined to Hebrews, very few of the cases reported being those of Jewish children. This was called the *juvenile*

type of amaurotic family idiocy to distinguish it from the infantile, peculiar to the first year of life, and as more cases came under observation the term *dementia* was often substituted for *idiocy*, as more precisely describing the character of the cerebral changes.

It is not my purpose here to discuss the relationship between the infantile and juvenile types of Tay-Sachs' disease. Torrence (6) a Glasgow physician, has discussed this relationship at much length in a recently published article, and comes to the conclusion that the two types cannot be sharply differentiated, the same family sometimes producing both types in different individual members. In particular he considers the positive assertion made by Sachs that the infantile type *invariably* occurs among Hebrews while a great majority of the reported cases of the juvenile type occur among non-Jewish children, thus making occurrence among Jewish children one essential factor in the diagnosis of true infantile amaurotic family idiocy. In opposition to Sachs' assertion Torrence cites a well-authenticated case of a non-Jewish infant who presented the symptom-complex of infantile Tay-Sachs disease. Several modern textbooks on pediatrics, as for example, that of Ashby and Wright, and Feer, agree with Sachs' viewpoint, as do also those on ophthalmology, Parsons, Graefe-Saemisch and Knapp.

Falkenheim (7), in a review of this subject in 1901, mentions that from a record of thirty-six families, four cases occurred in Gentiles. These cases, however, have not been verified by authorities according to the reports in the literature. Dr. Heveroch, in the *Neurologicher Centralblatt* of 1904, quoted eighty-six cases of amaurotic family idiocy of which forty-four came from America. Of these, sixty-one are reported as occurring in Jewish children, seven in non-Jews and seventeen no denomination mentioned. Dr. Aperts, in the *Handbuch der innerin Medicin* (*Erkrankung der Nerven System*, 1912), quoted one hundred and six cases of amaurotic family idiocy, only two of which occurred in non-Jews. Whether these latter reports included only infantile types is not stated.

Since Falkenheim's review in 1901 mentioned above, I have been able to collect from the literature only two cases of infantile amaurotic family idiocy in non-Jewish families. Cock-

ayne and Attlee (9) in 1914 reported before the Royal Society of Medicine, the case of a child aged one year. The parents were English, and first cousins. The members of the society who heard the report declared this to be a typical case of infantile amaurotic family idiocy "of the Jewish type," the condition described being identical with Tay's original one. Earl M. Tarr (8) published an article entitled, "A Case of Amaurotic Family Idiocy of non-Jewish Parentage, in the *Louisville Monthly Journal* for May, 1916. This report is from the Infant Hospital (Boston) the eye grounds were examined by Dr. George S. Derby of Boston. The second case (three patients in one family), was reported by Professor V. Starck (10), (Kiel), in the *Monatsschrift für Kinderheilkunde*, 1920. The report in the literature of these two latter cases of infantile amaurotic family idiocy in non-Jewish children speaks for its occurrence despite its rarity, and warrants the report of my case, mainly from the standpoint that it appeared in a child of non-Jewish parents and grandparents.

C. B., an Italian female child aged fourteen months; born in New York City, the parents being both born in Sicily. The grandparents also born in Sicily, were first cousins. This family history was substantiated by a thorough investigation. The father is a laborer. There is no history of lues or tuberculosis in the parents.

The patient was sent by Dr. Magner of Hackensack, New Jersey, to the pediatric service of Dr. La Fêtra at the New York Post-Graduate Hospital on October 25, 1922. The mother has given birth to five children with no abortions nor instrumental deliveries. The first child died at twelve months, the second at fifteen months, the cause of these deaths not being ascertained except that the parents say it was a disease similar to that now suffered by the present sick baby. They also remarked that the physicians in Italy were unable to tell them from just what disease the older babies died. These statements can only be taken as suggestive of the cause of death being amaurotic family idiocy or some allied disease. The third and fourth children, their ages now being five and seven years, are still alive and have always been healthy. The fifth child is considered in our case-report.

The child was delivered normally and breast fed for a year. For four months after weaning, the infant appeared to be perfectly well, like other infants of her age, from in-

formation gained of neighbors and the parents of our patient. The child then gradually became disinterested in her mother and surroundings, could not hold her head steadily nor sit up like other children; she appeared apathetic, was constipated and vomited at times regardless of the food taken; had snuffles, was a mouth-breather and had difficulty in respiration.

Upon admission the child looked pale, was poorly nourished and rachitic and not interested in her surroundings. Her face was expressionless, with broad nose, open mouth and—at times—labored breathing. The head dropped to either side when the body was raised and the child was unable to sit up or talk at the age of fourteen months. The head is of normal size, with the fontanels still open; the axillary and inguinal glands are palpable, there is beading on ribs; the heart and kidneys are normal; the spleen and liver are slightly enlarged; the abdomen pot-bellied; the ears normal, teeth decaying, tonsils enlarged; muscles of extremities of poor tonus and spastic; fists clenched; legs strongly extended; all deep reflexes increased, with no ataxia, no Babinsky nor Koenig signs.

The sound of clapping the hands caused twitching of the child's fingers and toes, but there is no hyperacusis. The skin is pale and loose. The reaction to galvanism and faridism is normal.

The laboratory reports result as follows: Wassermann reaction of blood and spinal fluid negative. Colloidal gold-reaction negative. Urine and differential blood count normal. Von Pirquet test negative. Temperature 97—Pulse 80—Respiration 26—.

On October 28, 1922, the child was taken from the hospital by its parents without the consent of the physician, but is still alive, and under observation though gradually becoming more feeble.

Eye Examination.—Externally the eyes appear normal; there is nystagmus with slow component to left when the head is turned to left; pupils moderately dilated, central equal, react sluggishly to light, and do not fix when a strong light is passed in various directions in front of the eyes. At a re-examination a week later the pupils were still dilated but did not respond to light, the eyes did not fix and vision was apparently *nil.* Fundus examination conducted under mydriasis and with the use of an electric ophthalmoscope was similar and symmetrical in both eyes. Papillæ show temporal pallor at first; later this was complete and sharply outlined, the ganglionic cell degeneration causing a secondary optic atrophy; the macular and perimacular area showing circular and grayish-white, with an ill-defined border;

in the center the fovea showing the characteristic circular cherry-red spot sharply defined in contrast to the surrounding whitish macular area. Retinal blood vessels, normal at first, at a later examination appeared to be slightly contracted. Otherwise the fundi were normal.

From these typical fundus findings, I naturally made the clinical diagnosis of amaurotic family idiocy. Inquiring as I usually do in these cases whether the patient was a Jewish child I was told that it was Italian and non-Jewish. I then asked for the clinical chart and further investigated the correctness of the family history, and was convinced that it was absolutely correct.

Before concluding I wish to mention several points which can be deduced from this report.

1. From a general examination of this patient, and the fact that these symptoms appeared in a non-Jewish infant, *unless* an ophthalmoscopic examination were made, the diagnosis of amaurotic family idiocy might have been missed.

2. Routine examinations of the fundi under a mydriatic and the use of an electric hand-ophthalmoscope are essential for aiding the diagnosis in general nervous diseases of *all* infants.

3. The fundus changes as described in this case substantiated the diagnosis of amaurotic family idiocy, as no other disease presents similar fundus changes, excepting bilateral embolism of the central artery, or hole in the maculæ, which naturally would not be considered in this case.

4. The report of this and other similar cases, should, I believe, change the accepted opinion of most investigators of this subject and also those set forth in recent textbooks, that infantile amaurotic family idiocy occurs exclusively and solely in children of Jewish parentage, although it does occur—according to our present reports—in the great *majority* of cases in Jewish children.

I wish to express my thanks and appreciation to Dr. La Fêtra for referring the case to me, and also to Dr. Magner for the many courtesies extended in permitting me to re-examine this patient.

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TUBERCULOMA OF THE ORBITAL CAVITY. EXHIBITION OF PHOTOGRAPH. LITERATURE.[1]

By Dr. DUNBAR ROY, Atlanta.

(With one illustration on Text-Plate VI.)

IN the last few years ophthalmologists have begun to recognize the importance of tubercular lessions of the eye.

If one will examine the ophthalmic literature for the last ten years he will be surprised at the number of articles dealing with this subject which is decidedly true of our own Transactions.

Most of these clinical reports have presented cases of localized tuberculosis of the conjunctiva, sclera, cornea, iris, choroid and retina, while but few have discussed the rarity of tuberculosis of the orbital contents or even an extension of the tubercular process from the interior of the eye to the surrounding tissues of the orbit.

In the mind of the writer the question of localized tuberculosis of the eye is far from being definitely settled.

Lesions occurring in the eye in conjunction with pulmonary tuberculosis, bone tuberculosis, or general tuberculosis in other parts of the body, where the tubercle bacilli or tissue changes showing a characteristic tuberculous histology by a pathologist eminently qualified to pass judgment on these findings, has an entirely different value as to a positive diagnosis, from the report of cases where the only diagnosis depends upon tuberculin reaction or the impirical qualities of being benefited by tuberculin injections.

In the large majority of cases of ocular tuberculosis, which have been reported, these have been treated for some time

[1] Read before American Ophthalmological Society, Washington, May 1922.

with other remedies both locally and through the system and when the case begins to improve under the injection of some form of tuberculin, we immediately place this case in the category of tuberculosis.

Then again it is strange that one observer should report such a large number of various kinds of ocular tuberculosis when another observer with equally as large clinical material sees so few.

Is this fact due to a faulty diagnosis by so many men who are practicing ophthalmology? The writer does not mean to imply that many of these cases reported are not tubercular but is it not a fact that we are prone to report an obstinate case as one of extreme rarity?

In the majority of observed cases of tuberculosis of the eye the diagnosis has been dependent upon tuberculin reaction since in the majority of cases the lesion was such as to preclude excision for microscopic examination and when we remember that the more certain diagnosis depends upon the injection or implantation of some part of the lesion into the eye or peritoneal cavity of an animal, we are confronted with the rarity of such diagnostic technique.

We look upon the presence of tubercle bacilli as the most certain diagnosis and yet how seldom have these microörganisms been found in a diagnosed localized tubercular process?

Next in importance must be the histologic changes seen under the microscope and here we are confronted with the rarity of such pathologic reports.

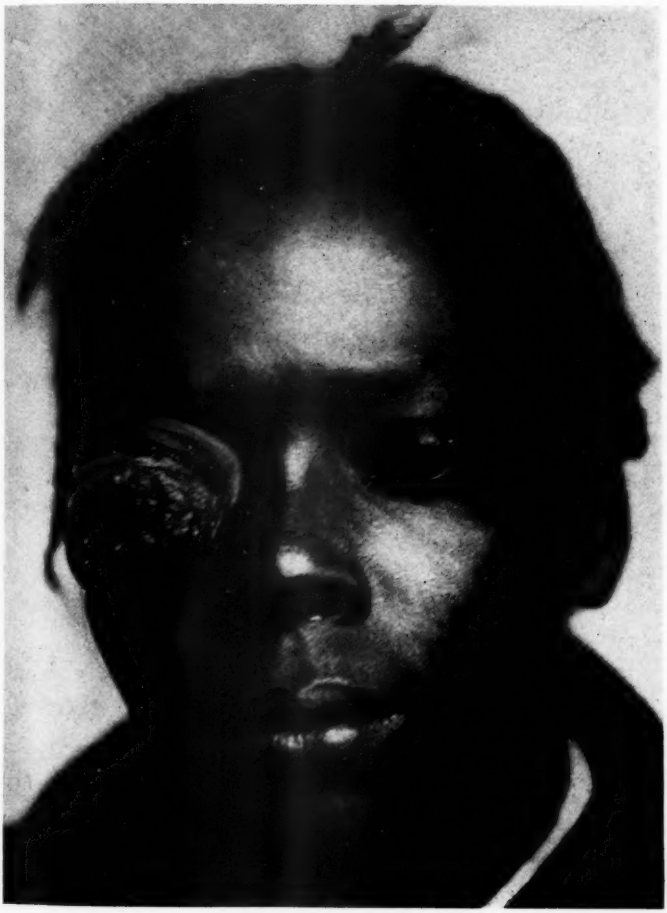
Many authorities say that a localized lesion means that there are other tubercular processes in the body, inactive perhaps but with grave possibilities for the future. Here again we may be dealing with uncertain deductions.

The writer does not intend by these remarks to be too incredulous as to the number of cases of ocular tuberculosis which have been reported but he does believe that when a case of this nature is presented the author should have exhausted all known clinical, serological, and histological tests before the same receives the stamp of authenticity.

Recently some very interesting articles have appeared dealing with ocular tuberculosis.

One by F. Schieck in the *Arch. für Ophth.*, June, 1921.

ILLUSTRATING DR. DUNBAR ROY'S ARTICLE ON "TUBERCULOMA OF THE ORBITAL CAVITY."



Tuberculoma of the Orbit

In discussing this subject he says that modern methods of examination in all these cases (ocular tuberculosis) will reveal in some part of the body evidences of preëxisting tuberculosis especially in the lymph nodes at the pulmonary hilus. This author distinguishes three different stages of tuberculous infection and tells us that as far as the changes existing in the anterior portion of the eye are concerned one is able to substantiate them in vivo by means of the Gullstrand apparatus. The success or failure of treatment with tuberculin depends upon what stage exists when the treatment begins.

In the Oct., 1921, issue of the *Transaction of the Biological Society of Paris*, L. Carrène also presents a very interesting article on the study of "Ocular Tuberculosis by Complement Deviation." In this article the writer calls attention to the fact that in a suspected case of ocular tuberculosis, syphilis should be absolutely excluded. He also makes the significant statement that ocular tuberculosis is rarely or never primary. It develops either concomitantly with lung, bone or other lesions or in individuals of tuberculous history.

Fuchs says that disseminated tuberculosis of the iris occurs as a form of iritis, that solitary tubercle of the iris as far as he has observed is confined to one eye, usually without iritis but resembling a neoplasm.

Von Graefe described it under the name of granuloma and Fuchs thinks that neoplasm is the correct diagnosis because the tumor keeps steadily enlarging and finally perforating the cornea near its margin and pushes out in the form of an exuberant growth.

Haab was the first to bring proof that these tumors were tubercles.

The only comparatively similar case was the one reported by Hansell in 1900. This was a tumor of the orbit in a girl of 13. It occurred beneath the upper lid and eye-ball. It was partly movable and attached to the roof of the orbit. The movements of the eye-ball were normal. The tumor was finally enucleated, measuring 3*cm* in length, 1.5*cm* in breadth and 5*cm* in thickness. Pathologic examination revealed evidences of the tuberculous origin of the growth. Hansell was unable to find a similar case reported in literature up to this time, 1900.

Investigating the subject further the writer finds that tuberculosis of the external adnexa of the eye and orbital cavity is extremely rare and in most of the cases reported it will be found that the tubercular process originated within the globe and the orbital involvement was secondary.

In my own case the pathologic report shows that the tuberculosis process originated outside of the eye-ball more especially around the optic nerve extending back towards the foramen opticus and that the tuberculomatous growth actually pushed in the posterior chamber of the globe.

As to the probable ætiology of this orbital growth it is difficult to say.

The nasal cavities showed absolutely no pathologic changes nor was there any history of previous nasal trouble.

Negroes are frequently afflicted with chalazia which break down and become infected. In this way there is a possibility of an extension through the lymphatics of a tubercular process.

The writer was unfortunate in not seeing the case until the condition was fully developed as shown in the photograph and where immediate operation was imperative.

CASE HISTORY.—Mary M., colored, age 19, consulted the clinic on Oct. 12, 1902.

Previous history:—Mother and father living. No history of tuberculosis in the family. Had always been strong and healthy. No history of syphilis although such statements are of no value among this race. Never any eye trouble until three months ago when the right eye began to pain a little and the white portion looked red. In a few weeks the eye began to look very prominent. From this time, the eye began to protrude and the sight gradually failed. There was present a membrane in front of the eye which looked like it was filled with water (evidently conjunctival chemosis). Complains of quite a little pain.

Examination:—Well developed girl with no glandular enlargements or body blemishes. Changes in the right eye-ball and orbital cavity can be readily seen as shown by the accompanying photo. There was intense protrusion of the whole orbital contents. The cornea could be seen. The bulbar conjunctiva was œdematous and thickened and extended far over the cornea besides protruding from the palpebral fissure. Palpation over the upper lid revealed a mass which was evidently filling the orbital cavity. Firm on pressure

and yet showing slight signs of fluctuation. Vision was of course destroyed. The other eye was perfectly normal.

The question of diagnosis was uncertain. The nasal examination was negative and there was no history of previous trouble. Operation was immediately performed by exenterating the orbital cavity without disturbing the lids.

The whole mass with eyeball was removed without difficulty, the optic nerve was severed close to the foramen opticus. The orbital cavity was swabbed with chloride of zinc solution and packed with gauze.

Recovery was uninterrupted. After the pathologist's report the patient was given all the clinical tests for tuberculosis without result.

She was seen two years after the operation and was in perfect health. Since then she has disappeared from observation.

Pathologist's Report:—Dr. John Funke, formerly Prof. of Pathology in Jefferson Medical College, Philadelphia:

"The specimen consists of a nearly globular mass measuring 4 by 3.8*cm* and weighing 15 gms. Its external surface is irregular as though dissected from other structures.

Although globular the specimen appears to be composed of two different structures, one a diseased eyeball and another rather firm homogeneous part around the optic nerve.

The greatly altered cornea can be recognized although blurred and only 0.8*cm* in diameter. Incision reveals the conjunctiva, retina and posterior chamber; the anterior chamber is obliterated. There is apparently little alteration in the retina, but the conjunctiva is much thickened.

The optic nerve is easily recognized passing through the homogeneous mass already referred to; it is around this nerve that most of the disease has taken place. At the origin and to one side of the optic nerve, the posterior chamber is pushed inward, due to the pressure exerted by the homogeneous mass. The diseased mass is dull, yellowish gray and most abundant midway between the origin of the optic nerve and the foramen. The mass is limited by considerable fibrous tissue which extends forward over the eyeball and to the cornea which structure has been partially obliterated.

Histology:—Section of the optic nerve shows evidence of œdema and considerable round cell infiltration in the sheath.

The mass around the optic nerve is composed in part of a homogeneous acid staining substance around which the tissue shows coagulation in which there are fragments of nuclei and cell detritus. There is considerable infiltration around the area of coagulation necrosis. Some of these cells are very large, have a hyaline acid staining protoplasm and nuclei which stain intensely with the basic dyes and are ar-

ranged around the periphery of the cell. Many of the sections show considerable fibrous tissue and circumscribed areas, the center of which show coagulation necrosis and the periphery composed of an abundant round cell infiltration. Among this cell infiltration there is clearly an effort made to produce fibrous tissue.

Diagnosis:—Chronic caseous tuberculosis.

In reporting the literature bearing upon this subject the writer has utilized only those cases where either an enucleation was performed and a pathologic examination made or where the history of the case was sufficiently uncertain in its diagnosis as to warrant some extended discussion:

Primary tubercle of the bulbar conjunctiva, followed by subacute pulmonary tuberculosis and death. Manuel Marin Amat, *Arch. de oftal. hispano-am.*, 21:233, Madrid, May, 1921.

The patient in this case was a young, robust man, with healthy parentage. During his military service he contracted measles, and two months later complained of a small neoformation of the left eye. This was the size of a pea, round, reddish-violet, very vascular, with a yellowish head. He complained of no pain or malaise except the feeling of a foreign body in the eye. The treatment consisted of lavage of isotonic serum, insufflations of iodoform powder, and, internally, elixir of guaiacol. Wassermann negative. Tuberculin cutireaction, strongly positive. The initial lesion was soon cured, but the patient began to be severely ill, with cough, expectoration, fever and emaciation. With hospital care he recovered sufficiently to rejoin his regiment but died four months later from pulmonary affection. This was evidently a primary lesion of the eye, acquired when in a sensitive state, when convalescent from measles. The infection spread by the lymphatic channels and became generalized. According to the literature, primary tubercle of the conjunctiva is a grave form of infection, with bad prognosis. Diagnostically, it must be differentiated from syphilis, mucous placques, sporotrichosis and from perikeratitis. The treatment is local and general; surgery is not indicated. Cautery may be used. Tuberculin must be used with caution but is indicated in localized lesions in order to immunize the organism against general infection. It is contra-indicated when there is great weakness, fever or hemoptysis.

A case of suspected solitary tubercular tumor in fundus oculi. Y. Onishi, in Nippon Gankagakkarzassi, 18, no. 3:

320–324, 1914; ref. *Ztbl. f. d. ges. Ophthal.* etc. 2:263; Berl. 1920.

Male, 23 years of age, suffering from catarrh of right pulmonary apex, was suddenly affected in July, 1912 with clouding of the lower portion of the visual field in the right eye. Positive Wassermann and Pirquet reactions. By the end of September a yellowish, light red, elliptical tumor had formed closely above the macula lutea. The ensuing ocular change measured 3*mm* in papillary diameter and lifted up the retina for about 4 diopters. The fovea centralis was surrounded by numerous small white spots forming a starlike figure. Large central scotoma. Treatment with iodide of potassium and by inunction continued for 10 months; gradual reduction of focus with simultaneous improvement in visual acuity from 0.1 to 0.4. Onishi believes this focus to be a solitary tubercle.

Tuberculosis of the choroid. L. Ortin, in *Arch. d. ophthalm. hispan. amer.* 14, no. 163:349–358; Barcelona, 1914.

Case Report.—Boy, 4 years of age; enlargement of right eye so that closure of lids is impossible; no ocular movement possible; eye directed downwards; sight = O. Bulbous protusions of sclera; no perforations; iris and crystalline lens normal. Eyeball contains a tumor of the size of a nut; the detached retina covers the tumor. The boy had several severe attacks of pain, and disease had been diagnosed as cysticercus or malignant tumor. After enucleation, the entire vitreous body proved to be one tubercular knob containing a caseous nucleus and numerous epithelioid and giant cells.

Two cases of solitary tuberculosis of the posterior bulbar portion. A. N. Natanson, *II. Klin. Mtsbl. f. Augen*, xlviii, 113–125, Stuttgart, 1910.

Case Reports.—1. Delicate but healthy boy; two years of age; slightly enlarged gland in front of left ear; yellow reflex in left eye.

Clinical ocular findings—left eye: cornea, anterior chamber, iris, crystalline lens, normal; pupil wide and fixed ("lichtstarr"); eye completely insensible ("reizlos") ocular fundus shows yellowish white reflex without special symptoms; increased tension; amaurosis; right eye: normal. Ocular diagnosis—retinal glioma.

Treatment:—enucleation of eyeball and excision of optic nerve almost down to optic foramen; recovery; dismissed 10 days after operation; further postoperative history unknown.

Microscopic findings—normal cornea with a few leucocytes in its posterior surface; central parts of anterior chamber shows normal depth; normal iris adheres peripherally to cornea and displaces angle of ocular chamber; normal crystalline lens; ciliary body slightly atrophic; a strictly defined and typically tubercular node in anterior temporal portion of choroid, rest of choroid to edge of tumor markedly atrophied; nasally *4mm* and temporally *6mm* from papillary area choroid begins to be uniformly inspissated and transformed into granular tuberculous tissue with epithelial and round cells, numerous giant cells and extended caseation; papilla is supplanted by a caseous tumor; papillary necrosis extends through lamina cribrosa to optic nerve; detached abnormal but non-tuberculous retina adheres centrally to tumor; posterior portion of sclera adheres firmly to tuberculous choroid; near opening of optic nerve the tumor has broken through and invaded the retrobulbar tissue; the excised portion of optic nerve shows necrosis of nerve trunk with tuberculous infiltration of sheath. A similar case is reported by J. Jung in *Arch. f. Ophthal.*, xxxvii, no. 4, 125–158, Leipz., 1891.

Boy, aged 2; scrofulous; yellow reflex in right eye.

Clinical ocular findings—left eye: normal; right eye: insensible; cornea normal; anterior chamber shows normal depth; tension normal; amaurosis; yellow reflex without special symptoms.

Ocular diagnosis:—glioma or pseudo-glioma; enucleation proposed but refused.

Clinical ocular findings two months later—right eye: both lids swollen; eye enlarged and protruding; slight clouding of cornea; shallow anterior chamber, iris tinged green; posterior synechia cause irregular pupil; pupil filled with exudate, tension probably slightly increased; ocular conjunctiva protrudes temporally at some *mm* from limbus; at tip of protrusion there is a perforation admitting the probe to the occular cavity.

Ocular diagnosis—intraocular tuberculosis, enucleation advised; at operation the ocular conjunctiva surrounding the perforation is left in place though a quantity of caseous matter is voided; the optical nerve is normal at the place of incision.

Postoperative history:—1 week after enucleation pneumonia set in; tuberculosis suspected and boy transferred to children's hospital; later history unknown.

Microscopic findings:—middle and deep cornea layers show diffuse small cell infiltration; hemorrhagic exudate in anterior chamber; hyperæmic iris with round cell infiltration; pupil filled with fibrinous exudate; pupillary edges adhering to

anterior surface of crystalline lens; ciliary body and posterior chamber transformed into tuberculous granular tissue completely walling in the crystalline lens; complete destruction of choroid, retina, lamina elastica chorioidea; the whole eye is filled with granulations containing round, epithelial and giant cells, many large tuberculous nodes with *rather few tubercle bacilli*. The center of the granulations is formed by a caseous focus; tuberculous granulations invade all layers of the sclera, infiltrate the ocular conjunctiva covering the sclera and extend through the papilla to the lamina cribrosa.

Tuberculous panophthalmia after confinement. M. Kellermann, in *Zrschr. f. Augenhlk.*, xx, no. 5, 464–467; Berlin, 1908.

Case Report.—July, 1907, admitted to Eye Clinic; married woman; aged 26; two healthy children; last normal confinement two months ago; two weeks after confinement inflammation of right eye set in; no trauma; swelling of lid and pus formation; swelling progressed gradually; rapid loss of visual acuity; no medical advice sought before admittance to clinic.

Clinical findings:—general examination negative; left eye; normal; right eye: marked œdema of conjunctiva; slight secretion; two scleral perforations near and just posterior to insertions of superior and external recti· perforations are as large as peas and yellow particles protrude therefrom; cornea absolutely clouded; no light reflex.

Bacteriologic findings:—secretion and chipped off necrosed particles negative.

Diagnosis made:—postpuerperal metastasis of apparently unknown ætiology.

Treatment:—enucleation of eyeball.

Microscopic findings:—numerous round cells, enlarged capillaries, leucocytes with lobular nucleus in conjunctiva; anterior chamber filled with fibrinous and granular tissue; sclera abnormally inspissated, with blood pigment between the individual lamellæ; perforations are bordered with granular tissue; cornea shows diffuse infiltration with various leucocyte cell types, no epithelial defect, no symptoms of past or present ulceration; iris and ciliary body are unrecognizable, four times their original thickness and transformed into granulations; crystalline lens cataractous; vitreous body, choroid, retina, and anterior uveal tract are transformed beyond identification and supplanted by granular tissue.

Histologic findings:—no leucocyte infiltration except in cornea and sclera; with the exception of the change in the crystalline lens the entire eyeball is one *giant tuberculous*

conglomeration perforating the thickened capsule of the eye in two places.

A similar case has been reported by De Lieto-Vollare, *Lav. d. Clin. ocul. d. R. Univ. di Napoli.*, v, 1897; in Lieto's case the retina also was slightly involved in the tuberculous process, and the course of the disease was sub-acute.

Primary tuberculosis of bulbar conjunctiva. W. Reis, in *Kl. Mtsbl. f. Augenhlk.*, xlv, 158–170; Stuttgart, 1907. Ten cases only reported in literature to 1904.

Case histories reported by:

W. Reis: Girl, 16 years of age; general history negative; in fall of 1905 right eye shows reddening of nasal portion, somewhat later a small tumor develops and gradually grows; April, 1906, admittance to hospital.

Clinical findings:—general examination negative; no enlargement of lymph glands; right eye: tumor, size of a pea, in nasal portion of bulbar conjunctiva; basis of tumor fuses into surrounding sclera; ocular conjunctiva covering tumor is flexible and locally markedly infused with blood.

Treatment:—medical at first, then enucleation of tumor; base of tumor was found to be so intimately fused with the scleral wall that tumor was cut from its base to prevent injury of the eyball; at the insertion of the internal rectus reddish gray gelatinous matter was found; wound sutured.

Postoperative findings—at end of April wound healed; at nasal end of bulbar conjunctiva painless, rosy, thick tumor, 1½*cm* at base; yellowish nodes scattered over surface of tumor; near limbus tumor shows operative scars; normal cornea and iris; crystalline lens transparent; visual acuity diminished to ⅓; pupil regularly enlarges after atropine instillation; vitreous body shows numerous uniform cloudings, papilla of optic nerve slightly hyperæmic; no changes in ocular fundus.

Histologic findings:—tumor sections show typical structure of tuberculous nodes with caseous foci.

Animal experiment made:—yellow node of bulbar conjunctiva excised and *intraperitoneally injected* into guinea pig; animal killed later; tuberculosis of mesenteric lymph glands and pseudo tuberculosis of spleen diagnosed at autopsy.

Tuberculin test:—made May, 12; injection of 1*mg.* "old Koch tuberculin"; general reaction; normal temperature fluctuations between 36.6 degrees and 37 degrees; after injection, evening temperature rose to 39 degrees and decreased gradually; specific ocular reaction; reddening and swelling of bulbar conjunctiva, hyperæmia of palpebral conjunctiva; palpebral fissure of right eye stuck together on next morning.

Walb—*first case reported* in literature; published in *Kl. Mtschr. f. Augenhlk.*, 1875. Case history:—young boy; scrofulous; caries of temporal bone with lymphomata colli; ocular findings: irregular conjunctival tumor in upper quadrant of bulbar equator; pathologic findings: tuberculous tissue; complications; panophthalmitis.

Wagenmann—reported in *Arch. f. Ophth.*, 1888.
CASE HISTORY.—Male, age 34; pulmonary tuberculosis; tumor, size of a pea, in lower inner quadrant near limbus; bacteriologic findings: tubercle bacilli; complications: peripheral clouding of crystalline lens; recovery after 5 months; 6 months later death from pulmonary tuberculosis.

Griffith—reported in Nagel's *Jahresber*, 1889.
CASE HISTORY.—Boy, age 4; lymphomata colli; ocular findings: thick elevation near limbus; pathologic findings: tuberculous tissue; complication; palpebral lupus; recovery after five months.

Rieke—reported in *Arch. f. Augenhlk.*, 1891.
CASE HISTORY.—Male, age 73, costal caries; ocular finding; tumor, size of pea, outside of limbus; bacteriologic finding negative; pathologic findings; tuberculous tissues; complication: tuberculosis of iris; later history unknown.

Moauro—reported in *Atti d. Acad. med. di Napoli*, 1897; cited by Saemisch in *Hdb. d. ges. Augenhlk.*, v, 1904.
Case history not given.

Uhthoff—reported in *Berl. Kl. W.*, 1900.
CASE HISTORY.—Girl, age 15; tuberculosis of nasal sinuses; ocular finding: round tumor, 1*cm* diameter, in lower inner quadrant adjoining limbus; pathologic finding; tuberculous tissue; positive tuberculin reaction; later history unknown.

Bossalino—reported in *Ann. di. Ottalm.*, 1901.
CASE HISTORY.—Girl, age 7; general examination negative; ocular finding: diffuse tumor, 4*mm*, thick, near outer limbus; pathologic finding: tuberculous tissue; no recurrence after seven months.

Puccioni—reported in *Ann. di Ottalm*, 1902.
CASE HISTORY.—Boy, age 8; general examination negative; ocular finding: round tumor, size of pea, at insertion of external rectus; bacteriologic finding: tubercle bacilli; pathologic finding: tuberculous tissue; no recurrence.

Chevalleran and Chaillous—reported in *Cong. d. l. Soc. franc. d' Ophth.*, 1904.

CASE HISTORY.—Male, aged 40; chronic bronchitis and testicular tuberculosis; ocular finding: thickened bulbar conjunctiva walls in entire limbus; bacteriologic finding: positive inoculation of rabbit results in peritoneal and iris tuberculosis; pathologic finding: diffuse infiltration without typical tubercular structure; later history unknown.

Lafon—reported in *Thèse de Bordeaux*, 1904.

CASE HISTORY.—Woman, age 22; tumor albus cubiti; ocular finding: tumor, 8*mm* wide, 6*mm* high, on temporal side of limbus and invading cornea; pathologic findings: fibromyxoma telangioma; recurrent tumor shows some caseous foci and giant cells; complication: punctate cataract; recurrent tumor four months later, also tumor albus carpi.

Solitary tuberculous tumor in papillary region of optic nerve: P. Verderame, *Klin. Mtsbl. f. Augenhlk.*, xlvi, 401–416, Stuttgart, 1908.

CASE REPORT.—Married woman; age 36; family history negative; right pleurisy with liquid effusion for five weeks; slight reddening of left eye previous to pleuritic attack; intense reddening and swelling of left eye since pleurisy; amaurosis; intense bulbar pain.

Clinical findings:—June 30 normal right eye: sight $\frac{6}{6}$ E; left eye: marked ciliary œdema; hyphemia of anterior chamber; plastic iris; gray reflex in fundus oculi; T. ÷ 1; eyeball painful to touch; LS = O; intense pain.

Treatment—pressure bandage; pain and tension diminished; July, 19 violent pains, eyeball enucleated in narcosis; marked hemorrhage into orbital tissue; July 29, complete palpebral ptosis; Aug. 2, faradisation; Sept. 11, no ptosis, palpebral levator functions normally.

Microscopic findings—tumor consists of *typical tubercles;* the detached retina adheres slightly here and there to the choroid, these adhesions prove to be chorio-retinal foci; posterior chamber and ciliary process are filled with fibrinous exudate; atrophic iris adheres with pupillary edge to anterior surface of crystalline lens, rest of iris protrudes; choroid shows thick diffuse infiltration throughout, numerous scattered Langhan's giant cells surrounded by epithelioid cells; suprachorioidal tissue shows thick nests of lymphocytes; pupillary area shows crater formation, filled with exudate containing detached pigment cells and detritus; at one place near the adhesion of capsule and pupillary edge there is a giant cell containing numerous irregularly distributed nuclei and pigment atoms; surface layers of

crystalline lens shows extensive decay; corneal endothelium is partially defective; anterior surface of cornea shows scattered lymphocytes; conjunctival portions of tumor show lymph vessels filled with leucocytes and numerous obliterated capillaries.

A rare case of epibulbar tuberculosis, R. Bergmeister, *Wien. m. W.*, lxxi, No. 24, 1045–1049, June, 1921

Bergmeister reports that anatomical findings of an enucleated eyeball from a man, 33 years of age, who was affected for years with recurrent "scrofulous" corneal and conjunctival inflammations. The eyeball showed superficial and deep corneal cloudings and 2 yellowish tumors about as large as half a lentil. Wassermann reaction negative; swollen glands in neck and axilla; former bilateral catarrh of pulmonary apex

Microscopic findings—complete scleral necrosis at site of tumors; conjunctival œdema; infiltration of lymphocytes, plasma cells, scattered typical non-vascularized tuberculous nodes with giant cells; also conglomerate tubercles; this infiltration spreads subepithelially deeply into the cornea, the canthus, into the anterior chamber along the pectinate ligaments and between the tissue of the iris.

Necrosis of the sclera is supposed to be due in this case to repeated tuberculin treatments causing excessive increase in antibody formation; œdema and partial necrosis of single retinal layers is said to be the effect of toxins.

THERAPEUTIC USE OF WEAK ATROPINE SOLUTION IN ASTHENOPIA.

By Dr. WILLIAM E. GAMBLE, Chicago.

EYE-ACHE and headache resulting from induced spasm of the sphincter iridis and ciliary muscle by the instillation of eserine is an everyday observation in our work, usually the discomfort being relatively slight; but in some cases much pain is produced. Recently one instillation of a ¼% solution of eserine in the eye of a physician produced so much eye pain that he had to be sent home in a cab and did not recover from the pain until the next morning. Part of our discomfort experienced in passing from a dark room into bright daylight is produced by the rapidly contracting pupils.

While with properly fitting glasses most persons can endure the accommodative spasm of their ciliary muscle in doing close work with but little pain or fatigue, there seems to be an increasing number of those who cannot.

I think you will agree with me that the rational treatment in these cases is to give less work to the tired eyes, to increase the nutrition of the patient and otherwise build up the general health. Unfortunately, many of them cannot quit work. Temporary rest may be given by instilling a high dilution of atropine which should not dilate the pupil enough to annoy the patient and should not interfere with close work. I have found $\frac{1}{100}$ of a grain of sulphate of atropine to an ounce of water dropped into the eye Saturday afternoons, for those who are doing close work the rest of the week, to give much relief.

If used oftener, the results are better.

I herewith narrate the history of three illustrative cases.

Case 1.—Mr. C. A. T., minister, 35 years of age. Came to me first in 1900. Said he had had sick headache as a child

which had continued up to that time at intervals of two to three weeks. He came to me especially on account of a "gripping feeling in his eyes when he did close work." He had worn glasses all his life without relief from this symptom. Had had to give up preaching two years before for six months. I fitted his eyes with proper lenses without any improvement in this pain in his eyes; finally as a last resort I prescribed atropine sulphate $\frac{1}{100}$ grain in an ounce of water. One and one-half years later he reported that he had used the solution continuously since seeing me, once or twice a week with relief from the "gripping" of his eyes. Later he reported that he could not use it that often as it had begun to produce irritation of the eyes. Finally he gave up preaching and went to farming, which cured him. The exaggerated contraction of the pupil in this case suggested to me the use of atropine.

CASE 2.—Miss L. T., aged 24 years. Referred to me by Dr. Henry L. Baker of Chicago. The patient is a seed analyst, using the microscope almost continuously during the day. She complained to me of eye fatigue. Could read only a few minutes without pain.

The correction of a small degree of myopia had no effect upon this symptom. Atropine solution was prescribed.

Six months later she reported that she had used the solution once daily with relief from the headache and that the medicine did not interfere with close work.

Advising her that the drug was not intended to be used indefinitely; but simply to tide her over the bad spells, I prescribed a pint of cream daily in addition to her other meals. A few months later she reported that she had gained ten pounds and could get along without the atropine.

CASE 3.—Oct. 27, 1904, Mrs. A. C. M., 30 years of age, referred by Dr. A. C. McIntyre, of Mendota, Ill. Complained of extreme photophobia and also of being unable to use her eyes in close work. She wore the proper lenses made of Crooks, noviol and other colored glass with but little relief.

I noticed in this patient also, the exaggerated contraction of the pupil on allowing light to enter the eye, and prescribed atropine sulphate. She reported to me a few months later that she had great relief by using this solution once or twice a week. She had seldom to use it three times.

Her pupil during this time was always larger than normal yet she evidently did not experience much discomfort from this dilatation.

It is not my claim that this treatment is anything but a stopgap until change of conditions or general treatment gives relief. I am not sure but that in many cases an even weaker solution might be indicated. In some cases a $\frac{1}{100}$ gr. solution was necessary to give relief. The strength and frequency of its use varies in different individuals. This particular solution is offered as a guide. Carelessness in filling the prescription should be carefully guarded against.

It would seem that the use of it is indicated more particularly between the ages of 18 and 35 years. In younger persons the stress and strain of life has not yet produced neuroses: in the older, the pupil becomes more sluggish with advancing years and the accommodation less, with the increasing sclerosis of the lens.

I am of the opinion that in many hysterical patients, the photophobia is of the trigeminal and not of the retinal type. The mechanical pressure on the nerve endings in and about the sphincter iridis is the source of the discomfort.

It is rare, in my experience to have seen indications for the use of this solution in men; practically all of the patients have been young women.

I am reporting my experience with this drug, hoping that indications for its use will be more carefully worked out by others than I have been able to do.

OIL CYST OF ORBIT.[1]

Removed by Kronlein's Operation.

By Dr. ARNOLD KNAPP, New York.

THE patient, referred to me by the courtesy of Dr. Hiram Woods of Baltimore, was a young woman 27 years of age who had had a protruding right eye for many years. The prominence had increased during the past year; it varied, and when marked was associated with pain in the eyes. The eyeball was normal and the eye was pushed straight forward. The vision in the affected eye was $\frac{20}{20}$. The exophthalmometer gave: Right, 26; left 17½. Motility of the eye was unimpaired. No change in exophthalmos on bending forward. The upper lid covered the upper third of the cornea; the lower lid was retracted exposing 3½*mm* of conjunctiva below the cornea. The scleral conjunctiva on the outer half of the eyeball was of a peculiar yellow color and congested. A firm mass was felt on palpation within the outer orbital margin. A definite diagnosis was not made and an exploratory operation was determined upon.

Operation Nov. 6, '20. Ether anæsthesia. After reflection of the soft parts externally, the bone was easily divided with the Hartley-Kenyon electric saw, with the kind assistance of Dr. J. H. Kenyon. The bone wedge was completed with a thin osteotome and mallet. On retracting the bone flap, the periosteum of the orbit was found uniformly bulging and tense. A horizontal incision was made in the periosteum, with an immediate escape of clear, oily fluid. On enlarging the incision more oily fluid, together with white sebaceous material, was obtained. The cavity presented a smooth and pink inner wall and extended from the conjunctiva back to the apex of the orbit. The sack wall proved so thin that it was very difficult to dissect it and some

[1] Read before American Ophthalmological Society, Washington, May 1, 1922.

had to be left behind. It appeared adherent in front to the region of the lacrimal gland. The external rectus was not encountered. Flap replaced; wound and eyelids sutured. Nov. 22, '20: the wound had healed by primary intention. There was some œdema of the upper lid. Nov. 27, '20: swelling of upper lid less. Vision normal. Exophthalmometer: Right 19; left 17. Motility normal. No diplopia. April 12, '21: there was a definite mass of thickened tissue to be felt under the outer margin of the orbit above the ligament. The conjunctiva presented a yellowish discoloration. The cosmetic result was satisfactory.

Microscopical examination. The cyst wall was composed of thin connective tissue without any papillary projections, an inner lining of several thicknesses of epithelial cells and keratin. The cyst wall contained very many sebaceous glands and a few hair follicles; in the surrounding tissues many dilated venules.

The oily fluids and solid material was examined by Dr. Theodore F. Zucker, of the Pathological Laboratory of the College of Physicians and Surgeons, who reported as follows:

"The oil contains no free fatty acids. It contains 36.2% of cholesterol and has an iodine number of 124. This would seem to indicate that it consists mostly of a triglycerid of a fatty acid, more unsaturated than oleic, the iodine number of the cholesterol being 56. It would seem that a fatty acid of iodine number about 180 were involved. While this oil was entirely soluble in fat contents, the solid material was not. The solid material contains 72% of cholesterol and gave an iodine number of 55. The alcohol insoluble portion was probably protein. It would seem then that while the oil is a triglycerid holding in solution 32% of cholesterol, the solid material is mostly solid cholesterol, containing as impurities some protein and very little of the oil."

Oil cysts of the orbit belong to the group of dermoid tumors, the proportion of oil contents depending on the preponderance of sebaceous glands. Lagrange states that their site of predeliction is in the prelacrimal region. In these oil cysts the oil is the direct product of the sebaceous glands. Some atheromatous material is always present in the depths of the cyst. The oil is either very yellow, rich in oleates, or very white like glycerine, composed of stearates and glycerites. The unusual features in this case were the yellowish discoloration of the conjunctiva over the tumor and the extreme thinness of the tumor wall. The yellow color of the conjunctiva was of the same

color as the oily contents and was undoubtedly derived from it. The walls of dermoid tumors are usually thick and the dissection is, therefore, not difficult.

In the performance of the osteo-plastic resection of the outer orbital wall I want to point out the advantages of dividing the bone externally with the Hartley-Kenyon electric saw,[1] which consists in an electric motor held in the hand, to which the saw is directly attached. By protecting the orbital periosteum and soft parts by suitable retractors, the upper and lower section through the superficial anterior part of the outer wall of the orbit is quickly made; the wedge of the bone is then completed with an osteotome and the flap reflected back. The opening in the bony outer wall is then enlarged in the depth by a rongeur forceps, making a good exposure of the orbital cavity. After completion of the operation the bone flap is replaced and fits accurately and can be firmly wedged in place; healing takes place without deformity.

[1] *Annals of Surgery*, April, 1907.

BLOCKING THE MAIN TRUNK OF THE FACIAL NERVE IN CATARACT OPERATIONS

By MAJOR R. E. WRIGHT, I.M.S., Madras, India.

SEVERAL methods have been described for partially blocking the facial nerve and controlling the orbicularis. The method adopted in this hospital was described in the *American Journal of Ophthalmology*, June, 1921. It is very similar to the methods described by Van Lint and Villard, differing only in that the nerve fibres are blocked nearer the main trunk. It is most useful when carefully performed, but a more complete effect is frequently desired. It has, no doubt, occurred to numbers of ophthalmic surgeons that blocking of the main trunk of the facial as it leaves the skull would be the surest means of securing complete muscular flaccidity. I do not know whether such a procedure has been described. However this may be, during the past year I attempted in a number of cases to cause temporary blocking of the nerve near the stylo-mastoid foramen in its extra cranial course, using 2% novocaine in varying quantities from ½ to 2*cc*. Two routes were chosen: in the first the needle was passed from below upwards and inwards along the anterior face of the mastoid process towards the stylo-mastoid foramen until it abutted on the bone close the foramen or actually touched the nerve; in the second the needle was passed horizontally inwards and backwards just in front of the mastoid process and immediately below the bony external meatus. In the majority of cases the result was negative. In the few where it succeeded, the paralysis set in within 15 minutes of the injection and persisted for upwards of an hour when signs of recovery set in. The paralysis was absolutely complete and it was most satisfactory to

operate under such conditions. Pending investigation with a view to finding exact anatomical guides which will lead to a sufficient success rate, to make the above method practically useful, an attempt was made to inject the parotid gland itself where the nerve begins to split up into its original branches. This did not give nearly such complete or lengthy paralysis. The onset was inside ten minutes and the duration not more than twenty. The successful cases in which the trunk of the nerve was blocked illustrate the possibility of obtaining transient but complete facial paralysis which is of the greatest value in certain cataract cases. It remains to be seen whether one can lay down definite instructions for finding the trunk with practical certainty. This note is published in the hope that others may try to render the procedure so easy as to be available to any surgeon who wishes to perform a cataract operation with complete relaxation of the facial muscles established. I have to thank Mr. P. M. Sridharan of my staff for assisting me in preliminary anatomical investigations.

REPORT OF A CASE OF MELANOSARCOMA OF THE CONJUNCTIVA.

By Dr. ANTONIO S. FERNANDO, Manila.

(With two illustrations on Text-Plate VII.)

I WAS prompted to report this case for in the first place I consider it a rare affection, and in the second, I hope that what had happened to this patient may serve as a lesson to any physician who may handle a similar case.

V. M., of San José, Batangas, a Filipino woman, 37 years old, with dark complexion, was admitted to the Philippine General Hospital on March 27, 1921, with a pedunculated black tumor in the conjunctiva of the right eye. It started about two months before admission as a small mass in the limbus of the right eye, growing rapidly, but causing no pain nor any inflammation. The palpebral fissure appears almost closed when looking straight at the patient, because the upper lid covers completely the growth, this causing a bulging of the lid at the center. (See Fig. 1.) To expose the growth the upper eyelid has to be raised up and brought on top of the mass. This is rather soft, black, projecting from the surface of the eyeball at the region of the limbus. (See Fig. 2.) The growth is pedunculated but with a broad attachment. It measures about *2cm* in its largest diameter, is irregularly shaped but with smooth surface. The cornea, pupil, iris, and fundus are normal. Vision is impaired only because the mass overhangs the cornea. She does not give any history of bleeding while in her home but here in the hospital it bled once due to slight trauma.

The growth was excised, but as the black pigment had infiltrated a rather large area of the conjunctiva, portions of it were left intact. The wound was sutured, and healed up by first intention. Section from the growth was diagnosed as melanosarcoma by the pathologist (Dr. Miguela G. Baltazar).

As vision was only slightly defective, the patient refused enucleation of the eyeball. She was discharged eleven days after the operation with healed up wound, smooth conjunc-

LUSTRATING DR. ANTONIO S. FERNANDO'S ARTICLE ON "MELANOSARCOMA OF THE CONJUNCTIVA."

FIG. 1

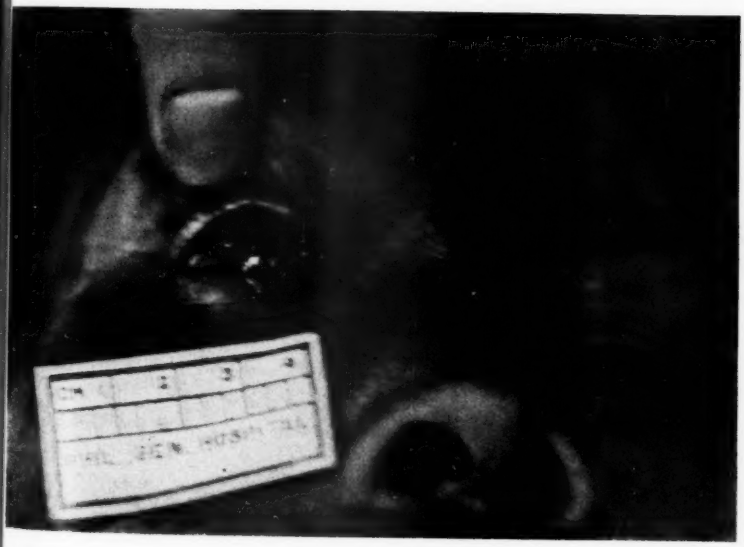


FIG. 2

tiva, but with portions deeply pigmented which could not be removed. The eye was not exposed to X-ray at all.

On January 16, 1922, about two years later, she came back to this hospital and was admitted to the medical department (by mistake) for generalized tumor masses in the skin, headache, dizziness, and ascites. The first swelling appeared just above the left breast about four months before this second admission, rapidly increasing in size. A few weeks later, similar swellings had appeared practically all over the body, and shortly after the abdomen became big and distended with fluid.

On admission there were found numerous nodular swellings, firm in consistency, not tender, varying in size from pea-size to two inches in diameter. The growths were subcutaneous and moveable, and were distributed all over the chest, trunk, and extremities, but there was no recurrence of the tumor mass in the eyeball, the conjunctiva remaining black as when discharged and vision remained the same.

Drs. C. B. Lara and A. B. M. Sison of the Medical Department, under whose immediate care the patient was in this second admission, had requested a section from the tumor just above the left breast, and the pathologists (Drs. Ernest Goodpasture and Eloy Pineda) reported "melanotic sarcoma."

The patient stayed ten days only in the hospital. While here she used to complain of severe headache, abdominal pain, dizziness, increasing ascites, and rapid emaciation, all of which could be explained by the metastases to internal organs. She was discharged with the advice to the family that the case was hopeless.

CONCLUSION.—In spite of its benign appearance, this tumor is malignant, and therefore, it is essential to extirpate the growth at the earliest possible moment, and if necessary, as it was in this case, to resort to enucleation even if the vision is not at all defective. In this case there has been no recurrence of the tumor mass in the eyeball, but rapid metastases had developed just the same.

You are all aware, however, how hard it is to persuade a very ignorant patient to have the eye enucleated even if it is greatly inflamed or already blind. We have had several cases of this experience among our laity. Knowing this you will not be surprised if we had failed to persuade this patient to consent to enucleation, and thus avoid a very unfortunate thing—the development of the metastatic growths.

A BRIEF CLINICAL SURVEY OF CASES IN THE FREE DISPENSARY OF THE PHILIPPINE GENERAL HOSPITAL.[1]

By Dr. ANTONIO S. FERNANDO, Assistant, Department of Ophthalmology and Oto-Rhinolaryngology, College of Medicine and Surgery, U.P.

MY object in presenting this paper to you to-night is to give some idea of the relative distribution of the common diseases of the eye, in our free dispensary, and also to state briefly some of my clinical observations on them.

A knowledge of this sort, I believe, will be of great help not only to the young specialist but also to the general practitioner here in Manila. As yet, there has not been published in the Philippines any clinical survey or statistical studies on eye diseases, and, consequently, the new practitioner has to depend largely upon statistics compiled in foreign countries where climatic conditions, mode of living, and even degree of education of the masses and other factors which influence the diseases, are different from what we find here.

Our free dispensary offers a very rich field for investigations of this nature. Indeed I consider this the best place at present in the whole Islands for research of this kind. Besides the ordinary facilities for diagnosis provided for in our dispensary clinic, such as a good refraction room, an adequate dark room, and other facilities, we have free access to the hospital laboratories, namely, the clinical and X-ray, whose staffs coöperate with us in making our diagnosis. Difficult cases are, as a rule, admitted to the wards for further study and proper diagnosis.

[1] Read before the Manila Medical Society, Dec. 12, 1921.

In the dispensary we come across all kinds of cases ranging from the very mild or incipient to the very advanced. In the hospital proper, we do not get these cases, inasmuch as those admitted are in the great majority of cases for operation only. We fail to see there cases which require purely medical treatment, as catarrhal conjunctivitis, hence, in compiling statistics of the relative distribution of eye diseases here, I have decided to gather my material from one source—the dispensary. Furthermore, we have occasion to observe cases after operation, for due to lack of sufficient beds in the hospital, patients are discharged early and the medical treatment continued in the dispensary clinic. We have the good fortune to follow up cases. Very chronic and perplexing diseases which have baffled specialists come also to our attention and give us hard but interesting problems to solve.

In the "group practice" as followed in the hospital, we have seen interesting cases referred to us from other departments of the Free Dispensary, and we begin to learn to look at their complaints from a broad viewpoint. Cases of subconjunctival hemorrhage in children which frighten the parents prove to be secondary to pertussis. Run down children, mostly with tuberculosis or with exudative diathesis, or those greatly weakened by a protracted course of ileocolitis, are referred sometimes from pediatrics for the marked photophobia of the eyes. It is not uncommon to see in these children xerosis of the conjunctiva, severe phlyctenular conjunctivitis, or keratomalacia. Cases of eye inflammation of apparently unknown origin, rapidly improved after the carious teeth have been extracted by the dental surgeon of the dispensary. Some cases of moderate impairment of vision among parturient women which cannot be improved with glasses are found to be due to gravidic nephritis or to beriberi amblyopia. Scores of such interesting cases can be enumerated. Furthermore, we begin to find more truth in the prophecy of Batten that "further progress in ophthalmology as far as one can see will be mainly on medical lines."

The following table represents roughly the relative distribution of cases. These numbers do not indicate the totals.

TABLE OF DISEASES.

Diseases of the Eyes and their Adnexa.

	1918	1919	1920	1921 (a)
Abscess, lids	25	25	23	24
Blepharitis	81	51	77	84
Cataract, senile	115	154	136	135
" traumatic	11	5	12	10
" juvenile	3	5	6	7
" glaucomatous	4	6	7	4
Chalazion	22	31	30	37
Conjunctivitis, catarrhal	720	575	609	649
" phlyctenular	285	274	226	271
" granular (trachoma)	45	98	161	113
" follicular	110	77	103	61
Dacryocystitis	82	116	140	130
Episcleritis	26	20	18	36
Foreign body, cornea	48	51	40	55
" " conjunctiva	47	44	74	66
Glaucoma	19	38	36	25
Injuries:				
Conjunctivitis, traumatic	56	66	50	—
Corneal ulcer, traumatic	—	—	—	—
Contusion, eye	28	34	40	—
Subconjunctival hemorrhage, traumatic	32	35	42	—
Iritis	6	17	29	22
Iridocyclitis	17	15	12	12
Keratitis (non-suppurative)	98	58	50	52
" traumatic	16	14	13	—
" interstitial (mostly syphilitic)	11	21	15	6
Leucoma	65	77	67	54
Macula	27	16	14	—
Nebula	16	10	20	12
Ophthalmia neonatorum	5	10	15	10
" gonorrheal	34	20	25	18
Optic neuritis	4	2	2	3
Optic atrophy	8	4	5	6
Panophthalmitis	31	29	20	11
Pertussis with subconjunctival hemorrhage	10	15	18	—
Perforation cornea with prolapse iris	7	6	7	3
Pterygium	107	76	103	121
Phthisis bulbi	25	18	21	10
Retinal hemorrhage	—	—	2	1
Symphathetic ophthalmia	—	1	1	1
Tuberculosis, conjunctiva	—	—	1	1
Staphyloma, corneæ	31	22	16	8
" sclera	1	2	1	1

TABLE OF DISEASES—*Continued.*

DISEASES OF THE EYES AND THEIR ADNEXA.

	1918	*1919*	*1920*	*1921 (a)*
Stye	145	138	161	238
Scleritis	6	10	6	4
Tumors:				
Cysts, lid	3	4	3	9
Glioma, retinæ	—	1	—	—
Lipoma, subconjunctival	—	—	1	—
Epithelioma, orbit	—	—	1	—
Ulcer, cornea (non-traumatic)	35	40	38	42
Xerosis, conjunctiva	10	12	14	11

BRIEF OBSERVATIONS ON SOME OF THESE DISEASES.

Conjunctivitis: This is the most common disease that we find in the dispensary. We have mostly the catarrhal, phlyctenular, follicular, trachomatous, and the gonorrheal conjunctivitis.

Catarrhal Conjunctivitis: The acute catarrhal predominates. Unfortunately extensive work for the determination of causative germs has not as yet been carried out due to lack of personnel. According to our statistics the disease shows no definite period of occurrence during the year as observed in other countries.

Phlyctenular Conjunctivitis: We find the great majority among children. Contrary to the general assumption that it has its origin mostly in children suffering from the so-called scrofulous diathesis, we find a large number of cases in apparently healthy children. Our statistics show that the disease has apparently no definite period of occurrence during the year.

Follicular Conjunctivitis: Usually found in young adults, majority among students and clerks.

Conjunctivitis Trachomatosa: The majority of cases have developed insidiously, and those whom the disease had attacked were not aware of it until their attention was called to it by certain physicians or nurses. The cases are usually discovered by health officers inspecting school children. Trachoma seems to be endemic in some of the towns of Cavite, as Imus, Naic, Kawit, and San Roque. Trachoma in

the cicatricial stage is quite infrequent. Eight cases only have been observed by me from Oct., 1919, until the present time.

Vernal Conjunctivitis: So far I have observed only one case of vernal conjunctivitis. The patient was a young man, complaining of photophobia and lacrymation on looking at bright light. The conjunctiva of the upper tarsus was covered with papillæ which were broad and flattened. The bulbar conjunctiva, however, appeared normal. The eyes presented a lesion very similar to a case diagnosed by a prominent ophthalmologist in San Francisco, California, as vernal conjunctivitis, and which we were fortunate enough to see.

Gonorrheal Ophthalmia: Most of the cases come from the city, especially from the district of Tondo. The disease is usually found in males. Out of 18 cases we had this year, 14 are males and the rest females; the males are usually infected by themselves from a urethritis from which they may be suffering at the time.

Ophthalmia Neonatorum: In the majority of our cases, infection has set in a week or so after birth. Subsequent infection by vaginal secretion of mother must have been the usua cause. Out of 10 cases observed this year, only one showed corneal opacities, and this happened because it did not receive any treatment for three months. Our table shows a gradual increase of the disease.

Pterygium: This is a common affection. Most of the patients are farmers and fishermen. The growth usually appears at the inner side of the conjunctiva of the eyeball. Two cases seen had marked impairment of vision as a result of extensive growth of the pterygium covering the pupillary area.

Cataract: Many of our patients are from the provinces, and the great majority come with cataract already matured or even hypermatured. Incipient cases come from the city and its suburbs. The age of the patient varies; the majority of those having senile cataract are between 50 and 60.

Besides the senile cataract we have observed the following types: (a) Soft or juvenile cataract, (b) traumatic cataract, (c) glaucomatous cataract, (d) congenital cataract. Two cases of congenital cataract have been observed; one in 1919 and another in 1920.

Dacryocystitis: My findings in regard to sex and types con-

firm my conclusion in the paper I read before this society last year about this disease, *i.e.*, it affects women more commonly, and that the chronic suppurative type predominates. Many seem not to give much attention to the disease, for not a few of our cases have come only when there is already marked inflammation of the lacrymal region with a history of old standing epiphora. Cases with septic corneal ulcerations and hypopyon are usually found in males.

Keratitis: Non-suppurative keratitis in the forms of superficial punctate keratitis, interstitial keratitis, and pannus is quite frequent: 98 cases in 1918. Majority of cases of interstitial keratitis give positive Wassermann test.

Glaucoma: The great bulk of our cases began with acute inflammation of the eye accompanied by violent pain in the eyeball radiating to one side of the head. It is these cases which have misled many general practitioners, thinking that the case was a general febrile disease with headache, and have treated the case as such when active ocular treatment of glaucoma is imperative. Unfortunately, many of our cases come to us with vision already gone or almost entirely lost, and what we can only do is to relieve the ocular pain and intense headache which rob the patients of their sleep. They are so advanced that usually no satisfactory fundus examination could be made. Glaucoma attacks women more frequently than men. Many of the patients attribute the cause of the disease to taking a bath after having stayed up late on the previous night, or sleeping with the hair wet. I think this belief is universal among our laity. In fact almost all cases of eye inflammation and blindness is thought to be due to either one of these.

Injuries and Foreign bodies: The common forms of injury observed are contusion of the eye and corneal ulcer caused by some small foreign bodies, as dust particles. In this connection I wish to call the attention of the audience to the harmful effect of *kahig* practised by our *herbolarios*. ("Kahig" is the process employed by our ignorant people to remove any foreign body in the cornea. This procedure consists in lightly scratching ("kahig" meaning scratch) the foreign body usually with the tender end of the stalk of certain kind of grass called "ulikbañgon." No anæsthetic of any kind is used and the procedure is done without the least attention to asepsis. If

the foreign body is well imbedded in the substance of the cornea, not only that the foreign body is not removed but a severe infection and extensive ulcerations invariably result.)

Errors of Refraction: Because of the rapidly increasing number of patients that have to be attended to in the dispensary, extensive work on refraction can not be performed. Most of our cases are of presbyopia and compound hyperopic astigmatism.

New growths: In 1919 we observed one case of glioma retinæ, one of epithelioma of the orbit, and one of subconjunctival lipoma. Melanosarcoma was also seen in an old woman who later developed metastasis in the skin all over the body.

Conclusion: In conclusion we can say that conjunctivitis, hordeolum, cataract, and dacryocystitis seem to be the most common diseases of the eyes.

REPORT OF THE TRANSACTIONS OF THE OPHTHALMOLOGICAL SECTION OF THE ROYAL SOCIETY OF MEDICINE.

By Mr. H. DICKINSON, LONDON.

The meeting of the Section on November 10th took the form of a Clinical Evening. The Chair was occupied by the President, Mr. A. L. WHITEHEAD, of Leeds.

Cases and Specimens.

Mr. HUMPHRY NEAME exhibited and demonstrated two specimens of calcareous lenses which had become dislocated into the anterior chamber. Each of the patients gave a history of trauma, when probably the dislocation took place, and the calcareous deposits occurred later. The calcium content was demonstrated under the microscope.

Mr. Neame also showed, in a man aged 39, a case of retinitis circinata, which condition had been seen to gradually develop. First there was a hemorrhage, of about two discs diameter; three months later there was a swelling above this hemorrhage, and later still there was a gray-white coating on it. As it had remained constant three months, he did not regard it as a neoplasm. On the idea that it might be inflammatory, possibly tubercular, injections of Tuberculin were given, B. E., but no local exacerbation nor temperature reaction took place. Wassermann was negative, and there was neither sign nor history of syphilis. Other possibilities were a cyst of the retina, or exudative retinitis. His own feeling inclined to cyst of the retina, or exudative retinitis with a deposit, mainly fibrous, in the seat of a previous hemorrhage. He exhibited slides of a section from a case of the late Mr. Coats, in 1911,

who had the eye excised in 1921 by Mr. Greeves on account of a painful glaucomatous condition. The case seemed to show a connection between hemorrhagic retinitis circinata and exudative retinitis.

Mr. MALCOLM HEPBURN said many cases of **so-called retinitis circinata originated in the choroid;** the original inflammatory deposit occurred there, and the deposits were always more intense at the macula.

SIR WILLIAM LISTER referred to the case of a man who received a blow on the eye, and later developed a large subretinal hemorrhage in the region of the macula. It produced a plum-coloured spot. Gradually the hemorrhage absorbed, and disclosed a large choroidal rupture. There was seen a configuration of white areas, such as occurred in retinitis circinata, but as a mere temporary condition following the rupture. He believed that in retinitis circinata there was a low form of infection, which caused the change to become more permanent.

Mr. LESLIE PATON reminded members that the case of the condition shown recently by Mr. Williamson-Noble had a positive complement-fixation test to tubercle, and that Dr. Axenfeld strongly believed that many of the cases of vitreous hemorrhage in young people were tubercular in origin. The lesion in this present case might be tubercular, not a cyst. This view was supported by the PRESIDENT, who strongly suspected the tuberculous origin of spontaneous hemorrhages.

Mr. NEAME, in reply, said he thought there might be a number of causes of retinitis circinata, which he regarded as a physical sign.

Mr. MONTAGUE HINE showed a boy aged 6 with **congenital dislocation of lenses,** and asked advice as to what was best to be done. Some had advocated leaving such a case alone until later in life, meantime watching it and noting alterations in vision; others suggested operation, either iridotomy, iridectomy, or discission of the lens. He also asked what was the ultimate end of these cases. Did the patients survive until adult age, or did a complication supervene?

The PRESIDENT said he had operated upon two or three such cases, fixing the lens with one needle, and breaking it up with another. The cases did well in respect of the lens

operation, but the vision was always sub-normal, probably because there was some congenital amblyopia, which caused the lens to be out of place.

Mr. HARRISON BUTLER spoke of having operated on some cases of the kind by a method advocated in America, following a preliminary iridectomy. This he described. In a case he did five years ago there was now some shrivelling of the iris, but vision was now $\frac{6}{5}$. If these cases were left, in some there was dislocation into the anterior chamber, and glaucoma; in others the lens dropped into the vitreous and caused cyclitis.

Mr. GREEVES spoke of having operated upon cases with a Ziegler knife, and vision improved from below $\frac{6}{60}$ to $\frac{6}{18}$ or $\frac{6}{12}$.

Mr. LEIGHTON DAVIES said the decision whether to operate or not should largely depend on whether the edge of the dislocated lens lay outside the pupillary area when the pupil was contracted. If it came just to the pupil, the case was better left alone. In a young child it was better to do needling than a large operation like extraction.

Mr. LESLIE PATON showed a case of cavernous angioma of the orbit, with microscopic sides. The patient was aged 76; and there was no trace of anything wrong until she was over 70. He found a growth the size of a walnut, but it was encapsuled, and came away very nicely, without subsequent bleeding. At some stage in her life there had been a fracture of the upper margin of the orbit, and he wondered whether there was a connection between that and the much later development of angioma.

Mr. PATON also showed a case of recurrent detachment of retina after 17 years of reposition. Since 1904 the man had had quite a number of operations. The eye in which the detachment occurred was of normal refraction.

SIR RICHARD CRUISE related a case in his experience which had re-attachment of retina after ten to twelve years of complete detachment. There had been no shrinking, and therefore there was a readjustment of the retina to the concavity of the sclera. This also was in an eye of normal refraction.

Mr. R. A. GREEVES exhibited a man, 37 years of age, who had bilateral proptosis, dating from a year ago in one eye, and five months ago in the other. His trouble was double vision, especially on looking upwards. The question was

whether it was a case of Graves' disease; he did not think that was probable. There was a tremor of the hands, but no tachycardia nor thyroid enlargement.

The PRESIDENT and Mr. REA favoured the idea of exophthalmic goitre.

Mr. OLIVER showed a patient on whom he had done a very successful plastic operation for contracted socket. In order to obviate the continued discharge and subsequent contraction often seen in these cases, he removed the whole of the conjunctiva, including that of the lids themselves; in this case he took away everything down to the periosteum. The man could now wear an artificial eye. The method was applicable to cases of exenteration of the orbit, in which there was no need to remove the lids. If skin-grafting were resorted to, it was important to skin-graft the under surface of the lids.

The PRESIDENT congratulated Mr. Oliver on his result.

Mr. FRANK JULER showed a girl aged 15, the subject of macular degeneration associated with mental deficiency. The disease seemed to start at the macular region in both eyes. The vision had been very defective three years. Earlier the optic discs were pale, of the waxy type of atrophy. The pigmentary changes in the periphery were now more marked than formerly. There was no history nor sign of syphilis in the child, but the mother gave birth to a premature child, then to one which died in 14 days. Before her sight became bad, this girl was in the lowest standard at school, and now that she was attending a school for the blind she was unable to learn like the other children did. He asked for views as to whether this was a typical retinitis pigmentosa, or a very chronic syphilitic retinitis, with secondary atrophy of the nerve, or a case of Batten's cerebro-macular degeneration. There was no paternal consanguinity.

Mr. RAE showed cases of ruptured ligamentum pectinatum, and of gummatous exudation at the base of the brain, optic neuritis, and diplopia. In regard to the second case, he spoke of a case in which Sir Charles Ballance did a decompression operation. The Wassermann reaction was positive. Within a fortnight of the operation the papilloœdema had almost disappeared, the paralysis had gone, and the woman was now at work. Following the operation the patient was thoroughly

treated with anti-syphilitic remedies, the novarsenobillon being followed by mercury and iodide.

Discussion on the Differentiation and Prognosis of Arterio-Sclerotic and Renal Retinitis.

A combined meeting of the Sections of Medicine and Ophthalmology was held on Tuesday, 28th of November, under the chairmanship of the President of the Section of Medicine, Dr. G. NEWTON PITT.

Dr. H. BATTY SHAW, speaking from the medical side, said he had had the opportunity of studying the clinical aspects and the post-mortem findings in a number of cases in whom the heart was found, at the necropsy, to be hypertrophied, and the only way he could explain the facts the cases revealed was to jettison former explanations and seek others. Some of the observed cases died of uræmic symptoms, yet the kidneys did not show the changes usually described as occurring in them. Albuminuria was present in varying intensity, or it was absent, yet the kidneys presented no uniform appearances leading to the view that they were responsible for the former, or of the latter, condition of the urine. Nor did the changes in the retinæ reveal what form of kidney was present in the cases. Some of the cases which had shown signs of grave disorganization of the brain disclosed a brain which, to the naked eye, was normal, and its vessels presented no change in either middle coat or intima. The phenomenon known as hyperpiesis seemed to be directly associated with the cardiac hypertrophy they all presented, and it was very variable, and nothing had yet revealed why these fluctuations occurred. He had been taught to believe that this phenomenon was caused by arteriosclerosis, which, for the present discussion, he would limit to the change met with in the middle coat of the arteries. The question which arose was, How could the variable hypiesis be due to the stable arteriosclerosis? He believed there could be no such dependence, and he had to invoke the presence of a variable amount of poison in the blood to explain the variable hypiesis, as also the arteriosclerosis. This likewise got over the difficulty of explaining the correlation of many of the accepted signs of "renal" disease

when little or no actual renal disease was present. A break-away had occurred in regard to the nomenclature of kidney disease, and the kidney changes were now held more to be due to toxæmia resulting from bacterial action at a site remote from these organs. Changes in the intima of the arteries could be produced experimentally by the injection of bacterial toxins, and now it was claimed that the changes in the middle coat were of the nature of a chronic inflammation. His strong inclination was towards the toxic view.

Ophthalmic surgeons admitted that they met with difficulties in differentiating arteriosclerotic retinitis from albuminuric retinitis; they had also admitted that an arterio-sclerotic retinitis might be succeeded or accompanied by the signs of renal retinitis. Some ophthalmological experts were now prepared to concede that the changes in the retinæ in renal retinitis were toxic, and that the seat of origin of the toxic agents was pre-renal. So that, for them, even renal retinitis was a misnomer. Why did changes occur in the retina in arteriosclerotic retinitis? When the hemorrhage had passed off, no sign of ruptured retinal artery or vein had yet been demonstrated. He believed the hemorrhages were likely to be capillary in origin. Where did the white patches seen in arteriosclerotic retinitis come from? If they were formed from local elements, what provoked their formation? Surely the cause was not arteriosclerotic changes. Was not a blood-borne noxious agent more likely? A general infective agent seemed to be behind all the changes, even those in the middle coat of the arteries. It was said that renal retinitis was always bilateral, yet works by ophthalmic surgeons revealed that "renal" changes might be shown in one retina by unilateral papillœdema, conforming with the observation that blood poisons need not necessarily produce symmetrical changes. The question might well be asked, What was the source in secondary anæmias of the development of soft-edged white patches in the retina indistinguishable from the "cotton-wool" patches of renal retinitis? He thought it likely that the changes met with in arteriosclerotic retinitis were not due to the vascular change, but that the hemorrhages and white patches and the slight change in the disk differed only from those in renal retinitis in being called into operation

by a slower influence of blood poisons. It was more reasonable to look upon arteriosclerosis as a first effect, and arteriosclerotic retinitis as a later one, effects of a toxæmia which acted slowly and in minimal quantity, and when it acted in large bulk, the other type of retinitis resulted. But this latter needed a name other than renal, for the changes in the kidney might be minimal. For the terms now current he suggested "chronic," "acute," "late," "early," leaving for the future the investigation of the nature of the toxin concerned.

The Retinitis of Arteriosclerosis.

The debate from the ophthalmological side was opened by Mr. R. FOSTER MOORE. He said his object was to bring forward evidence supporting the view that in some cases of arteriosclerosis a distinctive form of retinitis was developed, due, in his belief, to a local vascular disease in the retina. These cases had usually been confused with those of renal retinitis, and it had been said that renal retinitis in the old was less serious prognostically than in the young. He set out to establish the following three propositions:

1. That the ophthalmoscopic appearances of the condition were, in large measure, distinctive as compared with renal retinitis.

2. That the retinal exudates were developed as a result of the local vascular disease in the retina.

3. That as to length of life and manner of death, this ophthalmoscopic condition implied a prospect in sharp contrast with that conveyed by renal retinitis.

He submitted a table of 47 cases of retinitis, most of which he had observed for a number of years, and giving many important features.

In regard to the first of his propositions, he said that in most cases of general arteriosclerosis the retinal arteries shared to such a degree that their condition was recognizable by the ophthalmoscope; certainly this was so in 70% of 44 consecutive cases seen at St. Bartholomew's Hospital. He believed exudates were due to a thickening of the coats of the arteries and a reduction of their lumen. In these cases he thought the local pressure in the retinal arteries was less than normal,

although the pressure in large arteries was raised. The areas of exudate, thought not pathognomonic, had features which rendered them in large measure distinctive. This form of retinitis was frequently unilateral; it was so in 28 instances out of 45. Still, evidence of disease of vessels was always present in the other eye. The unilaterality did not persist for very long. Individual spots of exudate could be proved to disappear and leave no trace; but usually fresh ones were simultaneously appearing. In two of the cases, disappearance of the exudate followed thrombosis of the retinal artery. The chief points in which the ophthalmoscopic appearances differed from those of renal retinitis were: the character and distribution of the exudate and the changes seen in it, the frequency with which it was unilateral, its association with severe retinal vascular disease, and the absence of œdema and of "cotton-wool" patches.

In support of his second proposition, he quoted the history and course of a number of cases. One, under the care of the late Mr. Marcus Gunn in 1908, had, at that time, extensive arteriosclerosis but no retinitis. Her urine was free of albumin and sugar. This was the condition until 1910. In 1911, she came under the late Mr. Coats, who found white glistening spots disposed radially round the macula, and albumin in the urine. When, in 1913, Mr. Foster Moore saw her, she had a blood pressure of 250*mm*, a cloud of albumin in the urine, and retinitis in each eye. In 1918 she had a stroke, and her blood pressure was 260*mm*.

With regard to his third proposition, it was true that few patients lived so long as two years after renal retinitis was discovered. Of Belt's 419 patients, 94% died within 2 years. But the prognosis was less grave and more uncertain than in renal cases. Cerebral apoplexy might, in such patients, occur at any time; on the other hand life might be prolonged for several years. As to the manner of death, in a considerable proportion it was from uræmia in renal retinitis. Exactly 50% of his own cases died of a gross vascular cerebral lesion.

In conclusion, he said the condition called for separate recognition, and he considered that the term "arteriosclerotic retinitis" seemed appropriate.

Mr. P. BARDSLEY said he had long held the views of Dr.

Batty Shaw on the toxæmic origin of retinitis and sclerosis, views which he had himself brought forward more than once. He admitted that the picture of arteriosclerotic retinitis drawn by Mr. Foster Moore was correct, but thought the description applied only to very chronic cases; stated otherwise the retinitis depended on the acuteness of the disease producing the sclerosis. But if the toxin was more drastic, or an exacerbation occurred, the resultant picture resembled closely that of the so-called renal retinitis. He quoted a case in support of this. There were four classical changes in renal retinitis:

1. Retinal œdema, resulting in radiating lines or a macular star.
2. The fatty spots.
3. The hemorrhages.
4. The high pressure signs in the vessels.

All these signs might be present in three groups of cases without albuminuria, viz., in intracranial pressures, in advanced arterial sclerosis, and in many toxæmias. As, therefore, these retinal signs occurred frequently without albuminuria, and the latter could only be diagnosed by urine analysis, the term "renal retinitis" ought to be abolished, as it was misleading. The ophthalmoscope showed there was a toxæmia causing high blood pressure and vascular inflammation, also whether there were sclerotic changes in the vessel walls. On this latter, prognosis largely depended. If such sclerosis was present he believed death was a matter of only months, possibly weeks. If there were but little sclerosis with the raised blood pressure, there was a prospect of fair length of life. The sclerosis was the index of the chronicity of the poison, not of its acuteness. He contended it was possible to detect sclerosis in the vessels when high blood pressure was not present, and physician and patient could be forewarned. He gave a striking illustration of this.

Mr. P. H. Adams (Oxford) described the case of a man with a wound in the hip-joint, who complained of blurred vision. He had typical renal retinitis, slight papillœdema, soft "cotton-wool" patches, and hemorrhages, with a stellate figure at each macula. Yet practically nothing abnormal was found in his urine. His wound was very septic, and he was extremely ill, but after amputation and free drainage he quickly recovered

both health and sight, and was still well. This showed that toxæmia could itself cause the condition known as renal retinitis, without the kidney being involved. He believed that Dr. Batty Shaw's explanation would prove to be the correct one. His experience as to the length of life of these patients agreed with that of Mr. Foster Moore. He was more convinced than ever that a prognosis could not be made on the eye condition alone. Further research on the matter should be carried out jointly by physicians and ophthalmologists.

Dr. ARTHUR ELLIS spoke of a preliminary investigation he had been conducting with two colleagues on this subject when he received the invitation to take part in this debate. It was concerning 19 cases showing retinitis in which an estimation of renal function had been made. All the patients, with one exception, had a high blood pressure; in only 3 was it less than 200*mm*, *i.e.*, in one it was 180, in one 160, in another 148. In this last case Mr. Goulden reported one hemorrhage and that both fundi showed central degeneration and thickening of vessels in both retinæ. In 8 of the 19 cases there was evidence of gross renal damage and loss of function, with marked retention of urea in the blood. In 6 of the 8 there was a fixation of specific gravity. Of those 8, 4 were now dead of uræmia, one of broncho-pneumonia, and one was now dying of obvious renal inefficiency.

In the remaining 11 cases there was very little evidence of gross disturbance of renal function; in only 2 was there retention of urea in the blood, and in none of these was there fixation of specific gravity. Only 2 of these 11 patients were known to be dead, one of cerebral hemorrhage, the other of myocardial failure. The important question was, Was one of these groups a further stage of the earlier group? Before this could be settled, there would have to be a large series of post-mortem examinations in cases which had been carefully observed and followed throughout their diseased life.

Dr. C. O. HAWTHORNE, in a careful speech, protested against applying to the conditions under discussion terms which assumed definite knowledge when such was, so far, lacking.

Dr. J. F. GASKELL expressed his agreement with Mr. Foster Moore's views on renal and vascular disease. Two conditions, of entirely different pathology, were concerned: one primarily

a disease of the kidneys, the other of the vascular system as a whole. With regard to the first of these, there were various stages of diffuse nephritis with which were associated the forms of retinitis called albuminuric. The second condition was a cardiovascular one, in which three factors always played a part: raised blood pressure, cardiac hypertrophy, and disease of small arterioles of certain organs. In the purest examples of this condition the vascular changes of a degenerative nature were confined to the small peripheral arterioles, the largest arteries being free from the change. The kidney involvement was never sufficient to make primary failure of this organ the cause of death; the latter was almost always due to the changes in the brain, cerebral hemorrhage being by far the commonest occurrence. It was difficult to know whether the arteriosclerotic changes in the arterioles were secondary to the high blood pressure, or whether the latter was a response to obstruction to the peripheral circulation through essential organs. He agreed, however, that the changes were due to a cause which acted on the circulation as a whole. He favoured the term suggested by Sir Clifford Allbutt, namely, hyperpiesis.

Resumed Debate on Arteriosclerotic and Renal Retinitis.

This debate was resumed at a joint meeting of the Sections of Ophthalmology and Medicine on Friday, December 8th, the President of the former Section, Mr. A. L. WHITEHEAD, occupying the chair.

Mr. ERNEST CLARKE re-opened the discussion. He said he thought the papers on this subject by Dr. Batty Shaw and Mr Foster Moore would prove to be epoch-making. The teaching many years ago, and until quite recently, was that high blood pressure was the cause, or one of the causes of "hemorrhagic retinitis," and patients were sent to a physician to have that pressure reduced. It was now seen that high blood pressure was but one of the symptoms; it might even be a protective measure. The best term for the condition was, probably, "hemorrhagic retinitis." With regard to the exudates which occurred, he asked where they came from, and what caused them. If they were due to toxins, why should they not occur in both eyes? If they were associated with a hemorrhage, the

last question was answered. It would be useful, in future, where hemorrhage was seen in one eye, to take the tension of both the patient's eyes with a tonometer. He asked whether Dr. Batty Shaw suggested that the thickening of the middle coat and the intima were followed later by degeneration of these coats. Even the oozing hemorrhages presumably must be regarded as danger signals, a first stage which, if allowed to continue, might develop into so-called arteriosclerotic retinitis, and later into renal disease.

Dr. W. N. GOLDSCHMIDT related a fatal case of pre-renal toxæmia showing the clinical symptoms or signs of chronic parenchymatous nephritis. He said the success of an attempt to distinguish between "renal" and other forms of retinitis turned partly on what symptoms and signs other than retinitis justified the labeling of a case "renal," and the case he quoted illustrated the difficulty of the problem. He also entered into the question of the effect of decapsulation of the kidney and other remedies.

The patient was a man aged 42, and he came complaining of swelling of legs and abdomen for six weeks; he also had shortness of breath on exertion and occasional headaches. His only serious illness had been an influenzal febrile attack in Egypt in 1918. There was no venereal history. He had marked œdema of abdomen, legs, and back, with ascites; blood pressure 132*mm*. There was some pleural effusion at both bases. He had pyorrhœa and abdominal meteorism, and there was great flatulence after meals. About 200*cc* of urine (sp. gr. 1030) was passed in 24 hours, and it contained 2% of albumen. There were in it red cells and numerous casts, but the urea concentration was about normal. Wassermann reaction negative, fundi normal. No progress was made under medicinal and dietetic measures, therefore decapsulation of a kidney was tried, Mr. Gwynne Williams carrying out the operation. The kidney was found to be of normal size & color. The intestines were pale, but there was no peritonitis visible. Four days later he passed 900*ccm* in 24 hours, and the œdema was somewhat less; 10 days after the operation it rose to 1,200*ccm*, the albumen being .36%. Within four days, however, it dropped quickly to 600*ccm*. As it was possible the increased output of urine might have been due to the

operation, it was decided to repeat it on the other kidney, and this was done seven weeks after the first; the capsule, which was not tense, was slit and retracted. Several pints of milky fluid—as in the first operation—were removed from the abdomen. The speaker related the clinical course in great detail; the end was death. The post-mortem changes were also detailed. The sections of the piece of kidney removed during life showed definite slight changes such as could be produced by a toxic agent arriving in the blood stream. The sections removed after death showed only slight changes in comparison with a normal kidney. Therefore the illness did not seem to be accounted for by the state of the kidneys. It was probably due to a pre-renal poison which caused exudation into the tissues.

Mr. LEIGHTON DAVIES (Cardiff) said ophthalmic surgeons agreed there was a distinct difference between hemorrhagic retinitis with sclerosis on the one hand, and retinitis associated with albuminuria on the other, and these were largely recognisable by the retinal picture. But it had to be remembered that all people were not cast in the same mold, and there would be different reactions to the same morbid process. Hence no clinical group could have hard and assigned lines given to it; there would always be borderland cases, consisting of abnormal types. The two groups of conditions differed also in the matter of prognosis as regards life, the expectation of life being definitely greater in the arteriosclerotic than in the renal cases. That a like toxin should produce different reactions in different persons had an analogy in the case of the pneumonia bacillus: in one there would be croupous pneumonia, in another meningitis, in a third synovitis. A kidney of disordered function might lead to retention of material which acted as a poison, yet it did not follow that what caused the nephritis produced also the retinitis. Of 15 cases of the arteriosclerotic type, only one showed hemorrhagic retinitis. The importance of blood pressure in the conditions under discussion had been made clear. He did not think knowledge was sufficiently wide and certain to embark upon a new nomenclature.

Mr. M. S. MAYOU showed, by the epidiascope, sections of arterial degeneration in the retina, of thrombosed central

artery following vascular sclerosis, of thrombosis of central vein, a vein blocked by a fibrous clot, and an inter-retinal hemorrhage which had destroyed the retina right through. He also depicted exudations into various layers.

Dr. G. NEWTON PITT, O.B.E., reminded the meeting that the changes which took place in the large vessels, the medium vessels, and the arterioles were independent one of the others. It was often assumed that in cerebral hemorrhage arterio-sclerosis was present, but there were autopsies on many cases of the kind in which the arteries, including the middle cerebral, were not extensively diseased. And the number of cases of cerebral hemorrhage with marked interstitial nephritis was quite moderate. What he had said, applied equally to the case of the retina, whose vessels closely approximated in size to those usually giving way in the brain. It was desirable to ascertain the relation between the cases which died of cerebral hemorrhage on one hand, and those who died of a condition in which there were retinal changes. The occurrence of cerebral softening and cerebral hemorrhage in the retinal cases raised the question whether the lesions were due to the rupture of a minute vessel, or to a thrombosis. In many cases, he thought, the latter was indicated. He agreed that the prognosis in the two classes of cases was quite distinct. In some cases having arteriosclerotic vessels he thought some of the tissues were suffering from too low, rather than too high, a blood pressure.

Dr. FEILING spoke of a study he had made of 30 cases from the standpoint of the physician, all the cases having been referred to him by his ophthalmic colleague. Only 5 of these were renal, their average age was 43.8 years, and all had well-marked bilateral retinitis. The average systolic blood pressure was 235*mm*, the diastolic 135. In the 25 in the arteriosclerotic group the average age was 63.3 years, and 15 of them were females. Sixty per cent. of these had unilateral retinitis. The average pressure of the blood in these 25 was 214 systolic, 118 diastolic. He discussed the various theories of causation, and asked attention to the mechanical form of causation, such as in a case in which marked visual defect occurred in as short a time as 12 hours.

Mr. J. HERBERT FISHER reminded the meeting that in 1915

he read a paper before the Ophthalmic Section on the retinitis of pregnancy, in which he advocated the use of the term "Toxæmic retinitis of pregnancy" instead of albuminuric retinitis of pregnancy. Obstetricians believed that pathological vomiting of pregnancy, eclampsia, acute yellow atrophy of liver, and the necrotic changes of the kidney cortex which accompanied the albuminuria of pregnancy were due to a toxin, and that this might be produced by perverted katabolic processes in the cyncytium cells shed from the chorionic villi and put into the maternal circulation. In the organs liable to attack the stress was on the blood vessels, hence hemorrhages were a conspicuous feature. It was reasonable to infer that the fulminating lesions in the retina in these cases, with the exudates, hemorrhages and œdema, were due to the same cause. Mr. Fisher also referred to that disease of later life, retinitis circinata. This was so chronic that its explanation on the basis of an alteration in the arterial tunics fulfilled every requirement without invoking an absorption toxæmia.

If the toxic explanation of both varieties were accepted, it was reasonable to expect that in the arteriosclerotic cases with efficient kidneys the toxin should be found abundantly in the urine but in low concentration in the blood; while in the albuminuric cases the toxin should be found in concentration in the blood but only sparsely in the urine. Perhaps pathologists could determine what the toxin was.

Dr. HARFORD said it appeared from Dr. Batty Shaw's introductory paper and from the remarks of subsequent speakers that there was no such close relationship between changes in the retina and disease in the kidneys as had been commonly held. This required a review of the situation, meantime refraining from giving the grave prognosis which previously held views suggested, for such a forecast might hasten the fatal issue. Probably the appearances in question were common to many forms of disease which caused changes in the periphery of the vascular system. He quoted the following from a paper read by Professor Hugh Maclean at a meeting of the British Medical Association:

"There are many subjects who show but little evidence of marked cardiovascular changes, but in whom the renal system is hopelessly inefficient. Conversely, it is not uncommon to

find patients with very marked cardiovascular changes in whom but little evidence of renal disease can be ascertained. These points must always be taken into consideration in estimating prognosis, for, in a general way, apart from such accidents as cerebral hemorrhage, the outlook in a patient with high blood pressure is not so bad if the kidneys are efficient. Indeed, such patients may enjoy comparatively good health for many years, even with a blood pressure as high as 200*mm* of mercury or even more. This observation explains the curious cases one occasionally finds quoted in the literature in which a history of high blood pressure of 250 or over, frequently associated with retinitis and other eye changes was not incompatible with the enjoyment of fairly good health for several years." He deprecated the continuance of prophecy as to the date of a sufferer's death when he had this disease, because of the "emotional trauma" set up. In a case of panic there might be a state akin to temporary paralysis, or, in passion, violent muscular tremors.

With regard to the changes in the peripheral circulation, assuming that, as Dr. Batty Shaw said, there was a toxic process affecting both kidneys and retina, the problem was that of the selective action of the various toxins causing changes in the various vital organs. There was much evidence to prove the profound influence of suggestion upon local inflammations and vascular disturbances, and he hoped the teaching of modern psychology would be considered in its relation to obscure problems of pathology.

Dr. Batty Shaw, dealing in his reply with some of the speeches at the first meeting, said the discussion had at least given an opportunity for a statement of claim to those who believed there was something behind arteriosclerosis which was also responsible for other changes, such as those met with in the retina when the blood vessels of that tissue were altered, and for similar changes in the retina when such vascular change was slight or absent. It encouraged those who looked for some agent responsible for both, in the blood circulating in the vessels. All that had been said against the view that arterial disease was responsible for so-called arteriosclerotic retinitis could be equally urged against the view that the contracted kidney was responsible for uræmia.

He thought a large proportion of Mr. Foster Moore's cases showed hyperpiesis because there was some pressor body circulating in the blood stream.

Mr. FOSTER MOORE also replied. He said it was clear to him that there was such a thing as a retinitis due to toxæmia, and retinitis might occur from local causes in the retina. In renal retinitis there were two factors at work: the toxic one, which showed itself by the "cotton-wool" patches and the fibrinous exudate in the retina; and the vascular factor, which was seen by the sharp dots mentioned, and by the hyaline degenerate in the external molecular layer of the retina. And both factors might be concerned in a case. He did not suppose the hemorrhages in the retina were due to rupture of large vessels; they were probably due to diapedesis from the capillaries, owing to the altered condition of the blood. And in these cases he thought the blood pressure in the small vessels was lower than in health, even though the blood pressure in the brachial artery might be 250*mm.* And in anæmia the hemorrhages came about in the same way, through impaired nutrition in the capillary walls due to the poor blood. Mr. Bardsley said "copper wire" arteries might disappear, but such an occurrence was outside the speaker's experience. In answer to Mr. Ernest Clarke, he thought the exudates were due to degenerative changes in the external molecular layer of the retina, owing to the impaired circulation in the retina.

He did not pretend it was possible to draw a hard-and-fast line between arteriosclerotic and renal retinitis. He did not think the hemorrhages were due to emboli in the retinal vessels; they were different from the hemorrhages associated with infective endocarditis. It would be found, on following cases up, that a considerable proportion of cases of severe retinitis developed detachment of the retina.

REPORT OF THE PROCEEDINGS OF THE SECTION ON OPHTHALMOLOGY OF THE NEW YORK ACADEMY OF MEDICINE.

By Dr. BEN WITT KEY, Secretary.

MEETING OF OCTOBER 16, 1922. DR. J. M. WHEELER, CHAIRMAN.

Dr. Isaac Hartshorne and Dr. Raymond Hawkins reported a case of **orbital cellulitis.** W. L., boy, aged 14 years, complained of pain and swelling of the right eye, of three days' duration. No history of injury or sinus disease.

The lids of the right eye were tightly closed and swollen. Erythema, tenderness on palpation. No motion of the globe in any direction. No deep circumcorneal injection. Pupil reacted, vision nil. Left eye normal throughout. Rectal temperature 103°. General examination, including X-ray of nasal sinuses and teeth, and lumbar puncture, negative.

On April 22d, two days after admission, an incision one inch long was made through the eyelid, just below the supra-orbital margin at the nasal side. The roof of the orbit was normal and no free pus encountered. On April 26th, a similar incision was made just below the supraorbital margin at the temporal side, but no free pus found even on extensive probing into the orbital contents. Temperature for the first week ranged between 102° and 105° rectal. On the eighth day it began to fall rapidly, and by the 9th was 100°.

At the suggestion of Doctor Alfred Wiener, intramuscular injections of 10*cc* of whole milk, boiled three minutes, were begun on fourth day. Leucocyte count rose from 17,000 to 17,700. The chemosis became less marked, patient was brighter, and general condition improved. Three days later another injection of 10*cc* of milk was given, and these were continued every second day until the temperature was normal.

The leucocyte count increased immediately following each of the earlier injections. No chills or sharp temperature reactions experienced.

On the fourth day after admission, vision improved to counting fingers at three feet, ocular movements increased, and the mental condition became clearer. Two days later (after the second incision) there was temporary increase of limitation of motion upward. At the same time, the mental condition again became cloudy and there were distinct signs of meningeal irritation, shown by a slightly positive Kernig, a positive Oppenheimer, and increased knee jerk on the left side. These signs disappeared in two days.

The eye gradually improved until on discharge, September 15, 1922, these findings were present: Corrected vision, right eye $\frac{4}{10}$; left eye $\frac{3}{10}$. Rotation practically normal.

This case was severe enough to classify as a thrombophlebitis, which is usually fatal. In consultation with Doctor Cutler and Doctor Wiener, the question of exenterating the ethmoids and the orbit was considered. Before leaving the hospital the tonsils were removed. They believe that the use of a foreign protein in the form of boiled milk saved his life. During the first ten days they fully expected that he would succumb. After each of the earlier injections the patient seemed less toxic and brighter, and there was a slight rise in the white count.

DISCUSSION: DR. ALFRED WIENER congratulated Dr. Hartshorne on his persistent and successful treatment of this case by means of non-specific protein therapy. He wished to appeal for more general use of milk injections in combating ocular infection.

DR. CLYDE E. MCDANNALD in discussion reported a case of orbital cellulitis followed by meningitis and death. The patient, a child, aged 5, was seen first September 30, 1922. History of boils and styes for the past six months. Marked swelling of the left upper lid with redness near the outer angle and considerable œdema of the surrounding tissues. Temperature 103°. Removal to a hospital was advised and there an incision was made into the upper lid which failed to release any pus. Under hot applications the swelling and œdema increased rapidly extending to the side of the head and

occiput. Thirty-eight hours later the X-ray indicated an involvement of the left ethmoid and on advice in consultation an external ethmoidal operation was made but again no pus was found. Temperature continued high and next day rigidity of the neck and limbs, followed that night by death. Cultures from the pus, blood and spinal fluid revealed staphylococcus aureus infection.

DR. C. BARNERT said it was his painful duty to put on record a case of general septicæmia with fatal termination, following an injection of the milk preparation, Aolan, but he added that the fault was not in the use of the preparation per se but in the inexcusable carelessness of the physician who persisted in employing a broken ampule in which the milk was curdled and undoubtedly septic after exposure to the air for an indefinite period. The victim, a young college man, had received eight injections of 10*cc* each with marked benefit, for a long-standing folliculitis of the lid margins and a general furunculosis, and desiring to continue the treatment without interruption of his college work, continued the injections under the auspices of his college infirmary doctors, where after three harmless injections, the deliberate injection of an open, infected ampule caused his death.

A case of **accessory lacrymal gland with cystic duct** was reported by DR. ISAAC HARTSHORNE and DR. RAYMOND HAWKINS.

M. I., girl, aged 15 years, complained of internal strabismus of the left eye. The mother had noticed, when the child cried, a swelling at the external canthus of the left eye. The swelling was never painful, gradually increased in size, never became red or gave any trouble. After crying the swelling disappeared in from one to two hours.

After careful refraction, she was admitted to the hospital, and on July 25, 1922, tenotomy of left inferior oblique was performed, to correct the upward and inward deviation. At the same time, under anæsthetic, the tumor at the external canthus became as large as the end of the little finger. It was excised en masse, and one suture taken in the conjunctiva. August 1, 1922, partial tenotomy of left internal rectus was performed. Eyes now perfectly straight with correcting glasses.

Microscopic examination of section by Dr. L. C. Knox as follows: "Section shows that about half the specimen consists of a solid mass of glandular tissue resembling normal lacrimal gland. There is slight focal infiltration with round cells, especially along the course of the smaller ducts. Very thin capsule. The remainder comprises a collapsed cystic duct lined with slightly flattened cuboidal epithelium and supported by hyaline fibrous membrane. A few striated muscle fibers and nerve filaments are included in the outer portions of this stroma. The wall of the duct shows a moderate degree of chronic inflammation, being much congested and infiltrated with round cells and eosinophiles."

DISCUSSION: DR. ISADORE GOLDSTEIN stated that study of the macroscopic and microscopic examination of the gland and its covering leads him to prefer the term "sheath" to that of capsule of the gland.

DR. S. A. AGATSTON had seen a case of double cyst of the lacrymal gland.

A case of **tuberculoma of the choroid** was reported by DR. CYRIL BARNERT. E. K., aged 35 years, one week prior to first examination (Jan. 3, 1921) complained of intermittent diplopia and distortion of objects. No pain, inflammatory signs or headache. Previous history negative.

Examination—Both eyes appeared normal in every respect except definite pallor of both disks, and in the macular region of the right eye a circular, sharply-outlined area, about *2mm* in diameter, dark green in color, adjacent to which were tiny extravasations of blood below and on either side. The vision was $\frac{20}{200}$, unimproved. Perimetry disclosed a small central absolute scotoma, with normal fields otherwise for form and colors. The left eye was normal; vision = $\frac{20}{20}$.

General physical examination by an internist showed no other abnormality. The Wassermann reaction was negative, as were the examinations of the urine, teeth, blood and accessory sinuses. A cuticular injection of old tuberculin $\frac{1}{2}$*mg* produced no reaction, but a second dose, three days later, of one and one half *mg* produced a wheal at the site of injection, a temperature varying between 101 and 102 degrees for 24 hours and slight ciliary injection in the right eye. Systemic treatment with tuberculin residue was thereupon instituted,

beginning with $\frac{1}{10000}mg$, increasing the dose every third day one quarter until $\frac{1}{100}mg$ had been given. Local treatment was limited to subconjunctival injections of normal saline solution, and instillations of dionin. Meanwhile the local lesion persisted, growing slowly in size, with persistent sanguineous oozing about it. Removal of the tonsils was recommended and performed without benefiting the eye. The course of tuberculin injections was repeated a second and a third time without arresting the process, in fact, during the third series, which is not yet quite completed, a fresh exudate from the choroid was observed on October 1st, increasing gradually until it completely overshadowed the older lesions, and presenting the striking picture of a dirty white fluffy mass in the macular region measuring one and one half disc diameters. The vision is now reduced to $\frac{10}{200}$.

The case is presented as a striking clinical picture, but more particularly as an unusual instance of the failure, so far, to control a tuberculous process in the choroid.

DISCUSSION: DR. A. E. DAVIS stated that the diagnostic dose given the patient was too large. In such cases where hemorrhages are already present in the choroid or retina, we should be extremely careful both in the diagnostic and therapeutic doses, that they be not too large—else increased hemorrhage may be brought about and permanent damage follows. Tuberculin given in small but gradually increasing doses should be carried out over a long period of time.

DR. BARNERT in reply stated that he gives ½, 1½, and 3*mg* and without any apparent harmful effects. Three full days intervenes between injections.

DR. GEORGE H. BELL presented the paper of the evening, **"Reform Diet as a Therapeutic Measure in Ophthalmic Practice."**

Dr. Bell emphasized that the "Reform Diet" is part and parcel of his remedy for the "Three T's." All patients must be given the "acid test" for the "Three T's" (teeth, tonsils and toxæmias of the intestinal tract).

He claims that gastro-intestinal disturbances and severe septic intoxication are, at times, brought on or aggravated by oral sepsis, diseased tonsils or wrong food combinations and not infrequently by all three. Before putting patients on

"Reform Diet," hygiene of the mouth and throat is insisted upon. He urges the eating of raw milk, raw fruits, green vegetables and salads.

The principle of the "Reform Diet," he explained, is dependent upon avoiding the mixture of heavy starches and proteins at the same meal as well as the reduction in the intake of sugars and sweets.

He refers to twenty-two cases of chronic simple glaucoma which he is treating locally with pilocarpine nitrate, and hot applications. Internally these patients get the "Reform Diet" and colon irrigations. None have as yet come to the operating table. We must not lose sight of the fact that glaucoma is not merely a local disease, that chronic simple glaucoma is the outcome in every instance of prolonged chronic autotoxæmia. The treatment of these glaucoma cases and the details of the diet will be published in full in a paper at a later date.

After five years experience with the "Reform Diet," Doctor Bell feels convinced of his stand in recommending it as a therapeutic measure in ophthalmic practice.

DISCUSSION: DR. R. H. ROSE stated that Dr. Bell in addition to impressing the Three T's, has, in an interesting and scientific way, stressed the importance of faulty diet as a cause of toxæmia.

The increase in the use of sugar from 9 to 90 pounds per individual in the past century means the derivation of one fourth to one sixth of the caloric value of our food from an article which, according to McCarrison, contains no vitamins, those originally in the sugar-cane being destroyed. Much of the other carbohydrates in use, such as refined cereals and flour products, is also lacking in vitamins and minerals. This is the reason the uncivilized are often better physically than the civilized.

One important point in Doctor Bell's diet is separation of heavy starches from heavy proteins. It has been long recognized (Hemmeter Strict Diet, page 196, 3rd Edition) that in hyperchlorhydria carbohydrate digestion is checked by HCL. Meat stimulates HCL, therefore interferes with digestion of carbohydrates, therefore take heavy starches when heavy proteins are not eaten.

A case of glaucoma seen with Dr. Bell corroborates his opinion. Some oculists had said the case was incurable. Removing an abscessed tooth, and placing him on a diet reduced tension to practically normal.

The author believes that high blood pressure is generally due to toxæmia. Its cause may often be found among the Three T's. It seems reasonable to put glaucoma in the same category.

Dr. Joseph L. Behan said that the Reform Diet of Dr. Bell is a well balanced routine of feeding, according to his concept of the physiology of digestion.

Certainly, if proteids are mainly digested in the stomach, and carbohydrates chiefly in the intestines, either our physiology or nature is wrong. From birth our stomachs are accustomed to a mixture of proteids and carbohydrates, and by the time adult life is reached, if this physiology be correct, some adequate adjustment is made by the human machine whereby these unphysiologic food mixtures are tolerated, for surely the majority of the human race cannot be invalids.

He believes that the benefit derived from the Reform Diet lies, not so much in the restoration of digestion to within physiologic limits, as to the production of a systematized routine of feeding, and the replacement of artificial by natural foods. If for no other reason it is worthy of trial. He prefers to confine the ætiologic factor to the alimentary canal, to find the offending article of food and then prohibit its use. As regards the intestinal tract, his efforts are toward the production of the normal stool by the most natural means.

Dr. W. E. Deeks congratulated Dr. Bell on his Reformed Diet in the treatment of various ophthalmological diseases. The first work done along these lines was by Dr. Reeder and himself in the Ancon Hospital, Panama, during the years 1910 to 1914, when they obtained brilliant results in the treatment of inflammatory conditions of the fundus of the eye by the use of a diet in which all saccharose and excessive starchy foods such as pastry, sweets, desserts, pies, puddings and cereals were eliminated. They limited their patients to a diet consisting of all forms of meat, fish, cheese, eggs and milk preparations; all forms of green vegetables, cooked and uncooked, all

kinds of fresh fruits; and limited the amount of bread and potatoes.

The results of their experiences were discussed with Dr. Bell in 1916, and he was glad to note that Dr. Bell had advanced along the same lines and has gone even beyond what was anticipated.

He believed that the ætiological factors referred to in connection with the Three T's have back of them the use of excessive amounts of sweet and starchy foods. He had had no experience with glaucoma.

Dr. A. E. Davis in discussion said that while he agreed with Dr. Bell in a great measure in what he said as to the regulation and limitation of diet in the treatment of certain diseases of the eye, he could not concur as to the exact method he recommended. To make any method of treatment effective, it must be so arranged that the patient will take the treatment recommended. He did not believe it possible to induce the majority of patients to eat all carbohydrates or starches at one meal, to the exclusion of fats and proteins; or vice versa, all proteins at one meal to the exclusion of starches. In other words, the method is impractical. A properly balanced mixed diet, in his opinion, would be just as easily digested and certainly more palatable.

Relative to the point made by Dr. Bell, that cases of chronic simple glaucoma do better on regulating their diet, than by operating on them, it is well known that this type of case, as a rule, does better without operation than with it, provided miotics are used at the same time. A regular diet alone will *not* control the glaucoma. He has had such case maintain their vision by the simple use of miotics for as long as 15 years, even without dieting the patient.

Dr. A. J. Quimby referred to the importance of iodides in food, and discussed the several theories attempting to explain their physiological action.

Dr. F. W. Langstroth referred to the effect of pelvic disorders and infections as a source of ocular disease and appealed for closer observation and study of this relationship on the part of the oculist.

Dr. Bell wished to thank Dr. Deeks for bringing to his attention several years before the question of sugars and sweets in diet.

In reply to Dr. Davis regarding acute inflammatory glaucoma, Dr. Bell claimed brilliant results with the same line of treatment followed in chronic simple glaucoma.

In reference to the stomach taking care of starches and proteids at the same meal, he stated that most people are sick at forty years of age or have had some serious operation. This he insists is due to the fermentation in the alimentary canal brought on by wrong food combinations (heavy starches and proteins). McCollum, he said, has proved in the laboratory with animals that this mixed diet is a failure.

BOOK REVIEWS.

I.—**Glaucoma et Glaucomateux.** Par V. MORAX, Ophthalmologiste de Lariboisiere, Librairie Octave Doin, Gaston Doin, Editeur, Paris, 1921.

This interesting work in sixteen chapters covers the subject of glaucoma in every detail in a manner to be justly expected at the hands of such a master as this author is known to be. The opening chapter takes up the definition and etymology of the term and then launches into a detailed history of the condition, and of the distinguished workers of bygone days in this field, mostly French. The second chapter has to do with the ocular tension and the means of accurately determining it. Twenty-five pages are given to illustrating the methods of taking the tension, the significance of each, and definite detail as to just how each method should be employed. The use of the fingers, the manometer, and the tonometer have their uses, but if a student or reader is left with a casual reference to these methods to guide him, his attempts to employ them or to interpret the findings of others employing them, will be far from satisfactory. Morax has appreciated this and has left nothing to the imagination. If we are to employ the fingers in the absence of instrumental means—there is a right way to do it. It is well shown here. In using the fingers we prefer the index fingers of both hands. The technic of the application of the Schioetz tonometer is well illustrated. On the subject of physiology and pathology, the author writes at length, illustrating the text in a commendable manner. The symptomatology is well handled, and the colored plate showing the colored rings seen by the patient when looking at a light is especially good. The illustrations and text concerning glaucomatous excavation of the nerve head are conventional. The chapter on Infantile Glaucoma is

particularly noteworthy, and more than is usually given to that phase of the subject. Traumatic glaucoma is likewise considered at length and many apparently minor details are given proper emphasis. The several varieties of secondary glaucoma are described in detail and the description carries with it the earmarks of experience. In considering diagnosis and prognosis, sixteen chapters are consumed, and are in conformity with the high excellence of the rest of the book. In the treatment, eserin, pilocarpin, jaborandi, adrenalin, dionin, bromhydrate d'arecoline, and others are disposed of early, and then the surgical procedures are taken up in detail. Iridectomy and sclerotomy are described and then "Sclerotico-iridectomie"—the operation we like to include under the heading of Elliot's operation. The Lagrange technic of "sclerotico-iridectomie" is given in minute detail. Here the illustrations, however, tell the story much better than the text. Holth's technic, in which a scleral punch is used, is also given in full. Elliot's technic, using the trephine to remove a portion of the sclera instead of making a section of the sclera and then using scissors to excise the apex of the flap thus produced as in the Lagrange, is rather meagerly described although the pictures are fairly good. If the descriptions and pictures here given are to be taken authoritatively, it would appear that the Lagrange meets the indications far better than either the Holth's or Elliot's operation. However, these pictures, as do so many in this operation in other works, fail to show the disturbed relations of the swollen conjunctiva and subconjunctival tissues caused by the subconjunctival injections of cocain, or novocain, and adrenalin. In case the technic given fails to afford sufficient iridectomy he shows the use of the keratome for enlarging the scleral opening (after trephining operations) and excising more of the iris. After all, the principles of the Graefe iridectomy are the only reliable ones. The Lagrange operation appears to admit of greater reliability than the Elliot, largely on account of the size of the scleral incision and resection. As a choice Lagrange would doubtless be accepted.

I regret very much that the distinguished author has not alluded to the operation for glaucoma as carried out by Lt.-Col. Herbert, of Brighton, England, formerly of India. His

operation is known as the uniform linear iris-free filtration. The reviewer has had a great deal of experience in the iris free drainage and has obtained excellent results in reducing and keeping down the tension. He is not in sympathy with Herbert and Holth in the iris inclusive operation. After all has been said and done it is the hand of the operator that makes for success in any operative procedure in glaucoma.

The entire work is worthy of the advanced student's careful perusal.

L. WEBSTER FOX.

NOTICES

The International Congress of Ophthalmology (1925).

At the International Congress of Ophthalmology held in Washington in April, 1922, Mr. Treacher Collins presented an invitation on behalf of all the Ophthalmological Societies of Great Britain and Ireland to hold the next Congress in London in the year 1925. The invitation was accepted on the motion of Professor Gullstrand, of Upsala, Sweden, seconded by Dr. Lucien Howe, of Buffalo, New York. A general committee consisting of representatives of the inviting Societies has since met and has formed an executive committee, empowered to make arrangements for the 1925 Congress. It is to be held in London during the four days, Tuesday 21st to Friday 24th July. The three official languages are to be English, French, and German. The subscription for membership has been fixed at the sum of £2. Invitations will be sent to the principal Ophthalmological Societies or other representative bodies in every nation, asking them each to nominate a delegate to the Congress who would be responsible for promoting its interests in the country which he represents, so as to endeavor to make it a great reunion of all those interested in Ophthalmology throughout the world.

The Executive Committee is composed of the following members:—Mr. E. Treacher Collins, Chairman; Mr. J. Herbert Fisher, Vice-Chairman; Mr. Ernest Clarke, Treasurer; Mr. Leslie Paton, 29, Harley Street, London, W., and Mr. R. R. James, 46, Wimpole Street, London, W., Secretaries; Mr. A.B. Cridland; Mr. J. B. Lawford; Mr. Humphrey Neame; Sir John H. Parsons, F.R.S.; Mr. A. H. H. Sinclair.

Ophthalmological Society of the United Kingdom.

President: A. MAITLAND RAMSAY, M.D.

ANNUAL CONGRESS, 1923.

The next Annual Congress of the Society will be held on Thursday, Friday and Saturday, 26th, 27th and 28th of April, 1923, at the Royal Society of Medicine, 1, Wimpole Street, W. I.

The arrangements will be as follows:

MORNING. **THURSDAY, APRIL 26th.**

10 A.M. to 12.30 P.M. ... **President's Opening Address.**
Papers:—Mr. R. AFFLECK GREEVES: "A Series of Consecutive Cases of Cataract Extraction by Barracquer's Method."
Mr. R. FOSTER MOORE: "A Series of Consecutive Cases of Cataract Extraction by Barracquer's Method."

AFTERNOON.

2.15 P.M. ... ... Discussion on "The Disorders of the Blood and their Ophthalmological Manifestations." To be opened by SIR HUMPHRY ROLLESTON, K.C.B. (President of The Royal College of Physicians), SIR FREDERICK ANDREWES, F.R.S., and Dr. W. C. SOUTER. The following also intend to speak: ——

EVENING.

5 P.M. ... ... Bowman Lecture. To be delivered by Prof. GEORGE E. DE SCHWEINITZ (President of The American Medical Association) on "Certain Ocular Aspects of Pituitary Body Disorders, mainly exclusive of the usual Central and Peripheral Hemiopic Field Defects."
Members will dine together in the evening.

MORNING. **FRIDAY, APRIL 27th.**

10 A.M. ... ... Discussion on "The Diagnostic Significance of Proptosis." To

MORNING.	**FRIDAY, APRIL 27th**—*Continued*	
10 A.M.		be opened by Mr. WILFRED TROTTER, Mr. HERBERT FISHER and Dr. ANGUS MACGILLIVRAY. The following also intend to speak: Mr. PERCY FLEMMING, ——
AFTERNOON.		
2.15 P.M.		**Visit to The London Hospital, Whitechapel.** Clinical Meeting. Members are invited to show cases of interest. The Hospital will be open for inspection, and the Medical Staff will contribute exhibits.
EVENING.		
8.30 P.M.		Demonstration by Members.
MORNING.	**SATURDAY, APRIL 28th.**	
10 A.M.		Business Meeting. Papers:—Dr. ANGUS MACGILLIVRAY: "Enucleation of the Eyeball under Local Anæsthesia."

N.B.—Members having specimens illustrating any of their papers are invited to bring them for demonstration.

Members desirous of reading Papers, showing Cases, or taking part in the Discussions, are requested to communicate as soon as possible with Mr. R. FOSTER MOORE, 91 Harley Street, W. 1.

Papers and Communications, subject to the judgment of the Council, will be printed in full in the *Transactions*.

Under the By-laws readers of Papers must not exceed twenty minutes, subsequent speakers ten minutes. The openers of the Discussions are allowed twenty minutes.

All Communications must be type-written.

J. F. CUNNINGHAM
R. FOSTER MOORE } *Hon. Sec.*